OLUME 60 SEPTEMBER, 1948 NUMBER 3

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The AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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American Roentgen Ray Society · *Forty-ninth Annual Meeting*
Palmer House, Chicago, Illinois
September 14-17, 1948

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 60 SEPTEMBER, 1948 No. 3

PNEUMOENCEPHALOGRAPHY IN THE DIAGNOSIS OF CEREBELLAR ATROPHIES*

REPORT OF FIVE CASES

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THE diagnosis of primary cerebellar atrophy usually offers little difficulty in cases where the gradual evolution of cerebellar ataxia chiefly affecting the gait is not associated with any evidence of affection of other systems or of any disorder of the cranial nerves. Such a conclusion is, however, reached by a process of exclusion of which the disadvantages become apparent when an unusual feature, such as, for example, a sudden onset following trauma, complicates the picture. Even a final autopsy verification of diagnosis is seldom attained, owing to the prolonged course of the illness.

The pneumoencephalographic findings on patients suspected of having primary atrophy of the cerebellum, but in whom intracranial neoplasm could not otherwise be excluded, seemed to suggest that air studies may serve as a useful adjunct in establishing an in vivo confirmation of the diagnosis of primary cerebellar atrophy. In the 5 cases presented here, the diagnosis could be established on clinical data alone but pneumoencephalography gave satisfactory confirmation.

Although the pneumoencephalographic picture presented by cerebellar atrophies has been previously commented upon, it seems pertinent to point to the paucity of reports of the use of this method of demonstrating a reduction in size of the cerebellum. Some[1] who have advocated the method have overlooked the difficulty presented by the fact that reduction in size of the cerebellum is not always in proportion to the intensity of symptoms. In the primary lamellar atrophy, the shrinkage of the cerebellum is slight and the disorder demonstrable only by the loss of Purkinje cells on microscopic examination of the cerebellum, whereas the clinical disturbances may have been quite severe. On the other hand, cerebellar agenesis and hereditary primary atrophy may show minimal clinical disturbance until a fairly advanced stage of the disease, though the pathologist finds only a vestigial cerebellar remnant has been present. Just as the actual loss of cerebellar cortex does not indicate any proportional loss of cerebellar function, so the apparent size of the cisterna cerebellomedullaris, as seen on a lateral film, does

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not necessarily give a true indication of the real size of the cerebellum in relation to the posterior fossa. The occasional uneven density of the falx cerebelli, restriction of the atrophy to the cerebellar hemispheres with relative integrity of midline structures, may easily lead one to miss the loss in cerebellar substance if this be judged solely on the basis of the apparent air content of the posterior fossa as seen on a single lateral film. Only a systematic study of infratentorial air pockets in stereoscopic anteroposterior, posteroanterior and lateral views will give a true picture of the depth and extent of these pockets, and hence, indirectly, indicate the extent of actual loss in cerebellar mass. Thus the presence of pneumoencephalographic evidence of cerebellar atrophy will act as a confirmation of the clinical diagnosis, whereas its absence can only be taken as suggesting that the parenchymatous degeneration might only be of an extent determinable by microscopic study. The clinical diagnosis can only be confirmed but not negated by encephalographic evidence.

The clinical criteria for differentiating one type of progressive cerebellar atrophy from another are quite unreliable and at best only presumptive. The clinical differential diagnosis is, as Déjérine puts it, "des plus délicats et rien n'est plus malaisé que de l'établir." We have no evidence of encephalographic criteria to aid in the differentiation though, on anatomical grounds, slight enlargement of the prepontine cistern might be expected to corroborate the presence of olivo-ponto-cerebellar degeneration. Among the cases presented here, Case I was considered tentatively to belong to the class of olivo-ponto-cerebellar degeneration, and encephalography did show a slight enlargement of the prepontine cistern. However, a similar enlargement was also present in 2 (Cases II and V) of the other cases. Thus, a definitive classification of the "type" of parenchymatous degeneration in considering any individual case still falls mainly within the domain of neuropathology.

TECHNIQUE

Since our avowed interest focussed on obtaining a complete visualization of the whole subarachnoid space and the structures outlined by it, it was consequently imperative that one should resort to a very thorough replacement of the fluid within these spaces by air. Thus in all 5 cases reported 160–220 milliliters of spinal fluid was withdrawn by the lumbar route and replaced by air without the application of positive pressure, the actual amount of the removable fluid quantity depending on the free flow of fluid under good pressure, on the patient's degree of discomfort, and on any change in vital signs. Proper premedication, in our opinion, is of paramount importance in preventing the patient's suffering any undue discomfort and in ensuring the safety, of what might otherwise seem a drastic procedure, even in patients whose age and physical condition (Case V) might have been deemed a contraindication.

The procedure followed was essentially that outlined by von Storch.[4] Nembutal 0.2 gram and morphine 10 mg. subcutaneously was given one-half hour prior to the lumbar puncture. Twenty minutes later atropine sulfate 0.6 mg. was administered by the same route. If this premedication resulted in a considerable fall in blood pressure, this was remedied by ephedrine sulfate 50 mg. given intramuscularly. Lumbar puncture was performed in the sitting position. The fluid was allowed to escape under its own pressure into a large syringe held horizontally, displacing the piston. Each removal of 10 milliliters of fluid was followed by replacement with 10 ml. of air, this procedure being repeated until the estimated quantity was reached. After each injection of air, the head was moved laterally, anteflexed and retroflexed, to allow the air free admission to the various basal cisterns and then to distribute itself evenly throughout the subarachnoid space. As soon as the required amount of fluid was replaced, the lumbar needle was withdrawn and anteroposterior, posteroanterior, right

and left lateral stereoscopic films were taken, usually with the patient in the recumbent position.

The headache resulting from the procedure was controlled by raising the foot of the bed, forcing fluids and giving codein and aspirin, and in all 5 cases the headache had disappeared within four to eight hours.

The procedure described by Robertson[3] for the visualization of the cerebellum carries two distinct advantages, i.e., a more direct view of the whole cerebellar silhouette, and the use of much smaller amounts of air, thus reducing the patient's discomfort to a minimum. Although we have not used this method, it does seem to recommend itself in cases where encephalography is resorted to with the sole purpose of demonstrating atrophy of the cerebellum and should find more widespread use in the future.

REPORT OF CASES

Case 1. C. L., Male, white, aged thirty-eight, electrician, was admitted to the Neurological Service of the Boston City Hospital on May 9, 1946, with the chief complaints of slurring of speech for five years, and diplopia and unsteadiness of three years' duration. The difficulty with his speech came on very insidiously, being first noticed by his friends who complained that the patient spoke "as if he had a hot potato in his mouth." The words were slurred, indistinct, and gradually assumed an explosive quality. About three years prior to his present admission the patient noticed the onset of transient episodes of diplopia, usually initiated on attempting to focus for some time at a distant object. These episodes would only last for a few minutes. At about the same time the patient noticed that his body would sway from side to side while he shaved in front of the mirror. Over the next two years this unsteadiness while standing gradually progressed, affecting also his gait and making it impossible for him to walk on a straight line. Friends who witnessed his staggering and unsteady gait had often unjustly accused him of being inebriated. During all this time there was no gross unsteadiness in the movements of his upper extremities. Five months prior to admission the onset of occasional brief episodes of dizziness when the patient lay flat on his back, made their appearance. At no time was there any headache, nausea or vomiting. There had never been any blurring of vision nor were paresthesias ever noticed. Bladder, bowel and sexual functions had always been normal.

Past history: The patient volunteered the information that since early childhood he had always had great difficulty in performing fine coordinated movements with his fingers, such as fitting a small screw into a little hole, etc. The use of alcohol was denied.

Family history was entirely negative for neurological disorders of any kind.

Examination on admission to the service disclosed a well nourished, well developed man, anxious to cooperate and quite reliable. The general physical examination was entirely negative. The blood pressure was recorded as 135/90 mm. On neurological examination the slurring of speech was most conspicuous. The words were at times unintelligible. His speech had an explosive quality trailing off at the end of a phrase in a slurred diminuendo. The pupils were equal, reacted to light and on accommodation. The fundi were entirely normal. Extraocular muscles functioned normally, and there was no nystagmus. The tongue was in the midline, showed no tremor or atrophy. The rest of the cranial nerves were normal. There was no weakness of any of the extremities. Reflexes were generally hyperactive but bilaterally equal. The plantar responses were flexor. No sensory impairment could be demonstrated, position and vibration sense also being intact. Finger-to-nose test showed bilaterally a very slight tremor at the end of motion. There was no past-pointing. Alternating movements were poorly performed. The heel-to-shin test showed a slight bilateral dysmetria. The patient walked with a broad base, was unable to walk on a straight line without swerving to one side or the other, and seemed to take great care in turning around, this movement being executed with studied care, the whole trunk and hips moving simultaneously as if placed in a suit of armour. Romberg's sign was absent.

Blood and urine studies were entirely within normal limits. Blood Hinton was reported negative. Non-protein nitrogen 30 mg. per cent. Lumbar puncture showed an initial pressure of 150 mm. water; the fluid was clear, colorless and contained no cells; Pandy test negative, total protein 14 mg. per cent, chlorides 711 mg., and

FIG. 1. Case 1. Lateral roentgenogram.

the gold-sol curve was flat. Spinal fluid Hinton and Wassermann reactions were reported as negative.

Roentgen examination of the skull, cervical spine, chest and abdomen was entirely negative.

A pneumoencephalogram was performed with the removal of 170 ml. of fluid without noticeable discomfort to the patient (Fig. 1, 2 and 3).

Patient was discharged on May 29, 1946.

CASE II. W. W., single, white, unemployed male, aged thirty-eight, was admitted to the Service on September 7, 1946, with a six year history of weakness of his legs. The patient had been a neurotic child with "asthma" up to the age of fourteen, and enuresis lasting up to the age of eighteen. About twenty years before his present admission the patient had become a confirmed alcoholic. However, it was only about six years prior to admission that he noticed the onset of unsteadiness in walking. His legs began to feel weak, and he had to walk with a broad base to avoid reeling and staggering from side to side. This unsteadiness progressed over the next three years to the point where the patient could not walk without support. There was no associated weakness or unsteadiness of the upper extremities. Headaches vertigo, nausea and vomiting were denied.

FIG. 2. Case 1. Anteroposterior roentgenogram.

FIG. 3. Case 1. Posteroanterior roentgenogram.

There was no disturbance of bladder, bowel or sexual functions.

The past history was negative except for several hospital admissions for treatment of acute alcoholism, the diagnosis of cirrhosis of the liver having also been established during one of these hospitalizations two years prior to the present admission.

The family history was non-contributory.

Examination of the patient disclosed an obese, sullen male in no discomfort. The general physical examination disclosed atrophy of the papillae of the tongue which had a magenta color, and enlargement of the liver which could be felt four fingers below the right costal margin, being smooth, hard, and non-tender.

The neurological examination showed no abnormalities of pupils, eye-grounds or of the cranial nerves. There was no nystagmus. The strength of all four extremities was normal. There was no demonstrable hypotonia. Reflexes were hyperactive and equal throughout except for an absent right ankle jerk. Plantar responses were flexor. No sensory loss could be demonstrated. Position and vibratory sense were intact. Romberg's sign was absent.

The patient had a fine tremor of the head in both the anteroposterior and lateral planes. There was titubation of the trunk and slight intention tremor of the upper extremities in the finger-to-nose test. Alternating movements were very poorly performed. The heel-to-shin and toe-to-object tests showed gross ataxia. The patient walked with a broad base and reeling gait, occasionally reaching out for support to keep himself from falling down.

Blood and urine studies were within normal limits. The blood Hinton test was negative. Lumbar puncture showed an initial pressure of 120 mm. of water, no cells, negative Pandy test and gold-sol curve, total protein of 14 mg. per cent. The cerebrospinal fluid, Hinton, and Wassermann tests were also reported as negative.

A pneumoencephalogram was done after removing 220 ml. of fluid, without any discomfort to the patient (Fig. 4).

The patient was discharged September 24, 1946, his condition being essentially unchanged.

Case III. D. B., male, white, unmarried, clerk, aged sixty-one, was admitted to the Neurological Service of the Boston City Hospital with a history of progressive unsteadiness of his legs, this condition having had an insidious onset about one year prior to the present admission. The unsteadiness was limited to the lower extremities and was not associated with any weakness. Although minimal at the beginning, being only noticed while stepping on and off side-walks, the unsteadiness progressed over the period of a year to the extent that walking became quite difficult, and the patient often found himself staggering from side to side. At no time was there any headache, vertigo, nausea, vomiting or difficulty with speech. There were no associated paresthesias, shooting pains or motor weakness. About six months prior to admission, the patient began to have difficulty in emptying his bladder. This became

Fig. 4. Case II. Lateral roentgenogram.

progressively worse. On admission to the Boston City Hospital, Genitourinary Service, he was found to have a marked prostatic hypertrophy. A transurethral prostatectomy yielded 16.5 grams of tissue which was identified as adenocarcinoma of the prostate on histopathological examination. Immediately before his admission to the Neurological Service a bilateral orchidectomy was also performed and the patient was put on stilbestrol.

There was no history of ingestion of alcohol.

The family history was negative for neurological disorders of any kind.

At the time of the patient's admission for neurological review on September 25, 1946, he had almost completely recovered from the operative procedures of which some local edema of the penis and scrotum were the only residual signs.

The general physical examination disclosed an emaciated, elderly male in no discomfort. The skin was pale and dry. There was an old injury of the right eye with resulting opacity of the lens, a fixed right pupil and almost complete amaurosis on that side. The rest of his physical examination was negative except for the physical sequelae of prostatectomy and bilateral orchidectomy. The blood pressure was 150/90.

His neurological examination showed absence of the pupillary reflexes on the right side due to the old injury. The left pupil reacted normally to light and on accommodation. Fundi and visual fields were normal. There was no nystagmus. The cranial nerves were intact. No weakness of any of the extremities was noticed.

Biceps, triceps, radial and knee jerks were bilaterally equal and normal. The left ankle jerk was absent. Plantar responses were flexor. Abdominal and cremasteric reflexes were present and equal. No sensory loss could be demonstrated. Vibratory and position sense were also intact. Romberg's sign absent. The finger-to-nose test was well performed bilaterally. No adiadokokinesis was evident. The heel-to-shin and toe-to-object tests were, however, very poorly performed, with marked ataxia and action tremor. The gait was broad based and ataxic, walking on a straight line being impossible. When asked to stand perfectly still, a tremor of the head and titubation of the trunk became quite evident.

Examination of the blood showed a red cell count of 3.35 million, white cell count of 7,150, hemoglobin 60 per cent, with a differential count of polymorphonuclears 75 per cent, lymphocytes 24 per cent, monocytes 1 per cent. The blood Hinton test was negative. Nonprotein nitrogen 50 mg. per cent, and serum total protein 5.58 grams per cent.

Urine analysis showed a clear yellow urine giving an alkaline reaction, with a specific gravity of 1.010, one plus albumin, no sugar, and with large amounts of leukocytes in the urine sediment.

Lumbar puncture disclosed an initial pressure of 180 mm. of water, with free dynamics. The fluid contained 8 red blood cells, no white blood cells, the Pandy test was negative, the total protein 11 mg. per cent, the gold-sol curve was flat, and the Hinton and Wassermann tests were reported as negative.

Roentgen examination of the chest showed no metastases, the heart was not enlarged but the aorta was tortuous and markedly sclerotic. There was an irregular, mottled density involving the second lumbar vertebra, the right pubis, ischium and ilium, consistent with metastatic carcinoma.

FIG. 5. Case III. Lateral roentgenogram.

Pneumoencephalography was performed with the removal of 180 ml. fluid. The patient suffered minimal discomfort consisting of a headache which persisted for eight hours (Fig. 5).

After the subsiding of his penile and scrotal edema, the patient was discharged on November 22, 1946, to a nursing home for terminal care.

CASE IV. P. Z., single, unemployed, Russian-born, white male, aged fifty-nine, was admitted to the Neurological Service of the Boston City Hospital on January 19, 1947, with a history of "nervousness" of six years' duration. The patient was allegedly quite well up to six years prior to his present admission when he noticed the onset of a coarse tremor of both hands becoming evident only when he tried to use his hands. He had difficulty in writing and in using his tools properly. He never seemed to be able to hammer a nail because he always missed the nailhead by striking the hammer to one side or the other of the intended spot. About the same time a slowness and stiffness of gait was noticed which had progressed consistently over the subsequent years rendering the patient quite ataxic, with staggering and occasional reeling to one side or the other. These symptoms had been getting progressively worse. For the past six years he had also experienced paresthesias described as water dribbling down his legs or ants crawling down his thighs. These had only been noticed at night time and lasted about a minute, allegedly coming on almost every night. There have been no headaches, vertigo, weakness, nausea or vomiting.

The patient had been using alcohol in considerable amounts up to the time of onset of his neurological symptoms.

The family history was non-contributory.

The general physical examination revealed a deviation of the trachea to the right with impaired resonance over the right apex anteriorly. Otherwise the physical findings were essentially normal. Blood pressure was recorded as 154/94.

On neurological examination the pupils were found to be equal and reacted normally to light and on accommodation. There was no nystagmus. The fundi and visual fields were normal.

The cranial nerves appeared to be intact.

The strength of the extremities was normal and equal. The biceps, triceps, radial patellar reflexes were equal and slightly hyperactive; the ankle-jerk on the right, however, was slightly less active than the left. Abdominal and cremasteric reflexes were present. The plantar responses were bilaterally flexor. No sensory loss could be demonstrated. Position and vibratory senses were intact.

The patient was noticed to have a rapid rhythmical tremor of the head, exaggerated by voluntary movements of the head. There was a coarse terminal tremor of the arms and hands during the performance of the finger-to-nose test. Alternating movements were very poorly performed. Past-pointing and the rebound phenomenon could be easily elicited with the usual tests. A generalized hypotonia of muscles, especially of the upper extremities was noted. The heel-to-shin test and the toe-to-object test showed definite cerebellar-type ataxia and dysmetria. The gait was broad based and unsteady. Walking on a straight line was not possible. Attempts at running were consistently defeated by the loss of balance and excessive staggering.

Blood and urine studies were entirely within normal limits. The blood Hinton was negative, and the non-protein nitrogen 34 mg. per cent.

Lumbar puncture revealed a clear fluid with an initial pressure of 70 mm. of water. It contained no cells, the Pandy test was negative, the gold-sol curve was flat, the total protein was 29 mg. per cent, with negative Hinton and Wassermann tests.

Roentgenograms of the chest and skull were negative.

Pneumoencephalography was undertaken with the removal of 210 ml. of spinal fluid and replacement by air (Fig. 6 and 7).

The patient was discharged on January 27, 1947, without any change in his original condition.

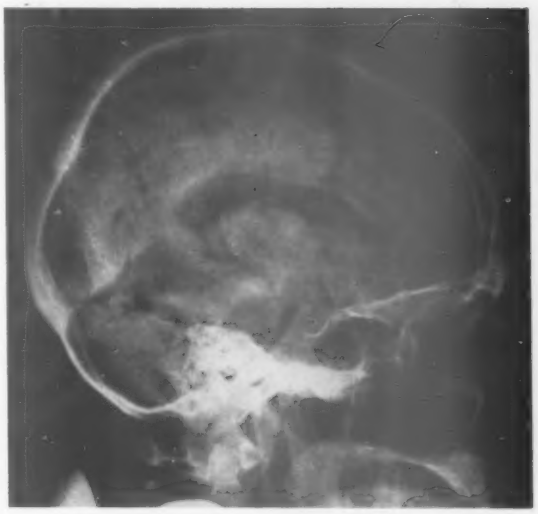

Fig. 6. Case iv. Lateral roentgenogram.

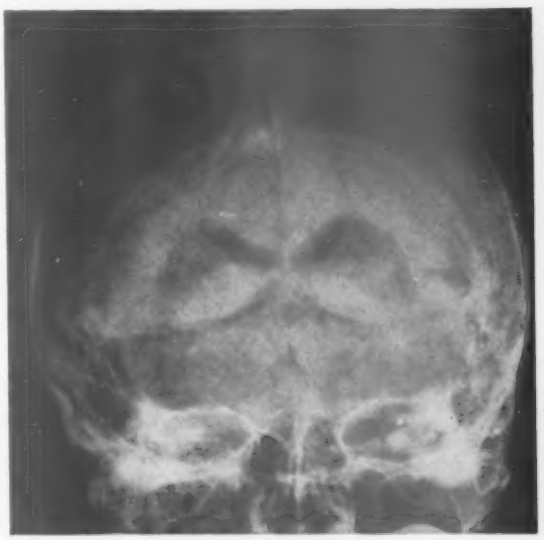

Fig. 7. Case iv. Posteroanterior roentgenogram.

Case v. J. H., a single, white male, aged seventy, was admitted to the Neurological Service of the Boston City Hospital on January 24, 1947, with a twenty year history of shaking of his hands and unsteadiness of his legs. The disease had begun insidiously, first noticed as a tremor of the hands as the patient reached out for objects. Soon unsteadiness in walking, occasional staggering, and swaying of the trunk while sitting made their appearance. There was no concomitant weakness, pain or headache. The disease had progressed steadily and had become very much worse about a year prior to admission, so that walking and shaving had become very difficult. The patient also complained of hoarseness developing over the period of one year. He also admitted a gross loss of memory for recent events, but could not indicate the time of onset of this symptom.

The past history was entirely negative. Ingestion of alcohol was denied.

The family history was non-contributory.

Examination disclosed a well developed, slightly emaciated white male, who showed the general ravages of senescence. Blood pressure was 142/56. The skin was atrophic and there was a mycotic infection of the toes. Marked

FIG. 8. Case v. Lateral roentgenogram.

generalized arteriosclerosis was evident. The cranial nerves were intact. There was no nystagmus. Laryngoscopic examination disclosed paralysis of the interarytenoid muscles with bilateral adductor palsy. Motor power was well preserved in all four extremities. Reflexes were bilaterally hypoactive, the ankle-jerks being absent. The plantar responses were flexor. Position and vibratory sense were reduced below the knees; otherwise there were no sensory changes. The patient presented the following evidences of cerebellar disease: there was a tremor of the head in the anteroposterior and lateral planes, this being markedly accentuated during walking. A coarse action tremor was evident in both upper extremities, not being limited to the hands but being also initiated at the elbow and shoulder. Adiadokokinesis was present as was also the rebound phenomenon. The heel-to-shin and toe-to-object tests disclosed gross ataxia in the legs. The gait was broad based, with occasional staggering and reeling from side to side. Attempts at walking on a straight line were constantly foiled by this unsteadiness.

Blood and urine studies were normal. The blood serology was reported as negative. Examination of the spinal fluid was entirely negative.

Roentgen examination of the skull and chest was negative.

Pneumoencephalography was undertaken after the usual premedication (Fig. 8); 120 ml. of fluid was removed and replaced with air. The patient recovered from the procedure uneventfully and was discharged on February 18, 1947, without any change in his condition.

Pneumoencephalography. Case I. The lateral ventricles are symmetrical, normal in size, and show no displacement (Fig. 1, 2 and 3). The third ventricle occupies its normal position in the midline. The aqueduct and fourth ventricle visualized in the lateral films are normal. The supratentorial subarachnoid markings are well outlined, indicating a possibility of diffuse cortical atrophy. The prepontine and perichiasmatic cisterns are well defined and large. Immediately under the tentorium there is an unusually large collection of air outlining the rostral or superior surfaces of the cerebellar hemispheres which present a rather pronounced concavity (Fig. 2 and 3) in contrast with the gentle ellipsoid slope that characterizes the superior contour of the normal cerebellum. The lateral films depict the relationship between the semilunar lobes and the dural lining of the posterior fossa. The maximum distance between cerebellum and bony density reaches 14 millimeters at one point. This space is continuous with the cisterna cerebello-medullaris which is about twice the normal size. The anteroposterior view emphasizes the reduced density below the tentorium. The whole picture is one of pronounced atrophy of the cerebellum.

Pneumoencephalography. Case II. There is a uniform dilatation of both lateral ventricles without any displacement. The third ventricle is moderately dilated but occupies its normal position in the midline. The supratentorial subarachnoid markings are slightly accentuated, indicating a moderate amount of cerebral cortical atrophy. The basal cisterns are rather large, as is the prepontine cistern. The posterior fossa holds an unusually large amount of air, the cerebellar silhouette being clearly outlined over its inferior surface by a large pocket which is continuous with the cisterna cerebello-medullaris beneath it (Fig. 4). The maximal distance between the inferior cerebellar surface and the cranial diploe opposite it is 14 mm. as measured on a lateral film. It was concluded that a definite reduction in size of the cerebellum had taken place, though the subtentorial space was not outlined as in Case I.

Pneumoencephalography. Case III. The lateral ventricles are symmetrically enlarged and show no displacement. The third ventricle is in the midline and perhaps slightly wider than usual. The subarachnoid markings over the surface of the cerebral hemispheres indicate a moderate degree of cortical atrophy. The posterior fossa is well filled with air, demarcating a definite enlargement of the cisterna cerebello-medullaris

both in width as well as in depth (Fig. 5). The infratentorial air pockets are also definitely larger than commonly seen, the whole picture being consistent with cerebellar atrophy.

Pneumoencephalography. Case IV. Both lateral ventricles are symmetrically and uniformly dilated, without any displacement or distortion. The third ventricle is in the midline and moderately enlarged. The cerebral sulci do not appear wider than usual and there is no evidence of cortical atrophy.

In the lateral view the superior surface of the cerebellum has lost its normal rounded silhouette and presents a concave surface (Fig. 6). In anteroposterior and posteroanterior views (Fig. 7) the amount of air between tentorium and cerebellum appears of normal, or only slightly increased, amount. The lateral recesses of the posterior fossa show large collections of air, indicating a definite reduction in size of the cerebellum. This atrophy is further emphasized by the accentuation of the individual outlines of the cerebellar fissures. The cisterna cerebello-medullaris is about twice the normal size, and there is a large collection of air between the inferior surface of the cerebellar hemispheres and the inner diploe of the occiput, the greatest distance between these being at a point 20 mm. beneath the tentorium where the cerebello-diploic space is measured as 15 mm. on the lateral film. Examination of the stereoscopic lateral films gave a clear view of the shrunken cerebellar outline in relation to the posterior fossa.

Pneumoencephalography. Case V. There is a symmetrical uniform enlargement of the lateral ventricles without any displacement. The third ventricle occupies its normal position in the midline and is dilated, slightly globose in shape. Widening of the sulci and the wide spacing that demarcates the insula shows the presence of marked cortical atrophy, the corresponding loss in white matter being reflected in the enlargement of the ventricular system. The interpeduncular and perichiasmatic cisterns are markedly enlarged, as is the prepontine cistern. The lateral stereo films emphasize decrease in the size of the pons. The posterior fossa is not fully occupied by the cerebellum. The cisterna cerebello-medullaris is unusually large, its lateral depth being accentuated by loss of cerebellar substance of the hemispheres (Fig. 8). The space between tentorium and upper surface of the cerebellum is doubtfully if at all enlarged. Stereo lateral films show a very clear demarcation of the folia cerebelli with large collections of air outlining each quite clearly, the primary and secondary fissures of the cerebellum being well defined. This appears as ample evidence of the parenchymatous degeneration of the cerebellum, although the total amount of subtentorial air, as observed on lateral views, appears to be less than that present in the previous cases.

DISCUSSION

The symptomatology of all 5 cases was more or less similar. The common features may be summarized as follows: The gradual onset of symptoms in males of middle age (except in Case I where the disease had its onset at the age of thirty) with no history of similar disturbance in other members of the family. The most common complaint was difficulty in walking with reeling and staggering in the more severe cases. Cerebellar asynergia, dysmetria and tremor were minimally present in the upper extremities of all 5 cases, these signs, however, being most conspicuous in the legs. In none of the cases was there any nystagmus. Dysarthria was observed in only 1 of the cases (Case I). All the patients walked with a broad base. The reflexes were recorded as normal except for an absent ankle-jerk in Cases II and V. In view of the assumptions previously made by Romano, Michael and Merritt[5] regarding the probable alcoholic etiology of cerebellar atrophy, a most careful scrutiny of the habits of the patients was undertaken. In only 2 of the cases (Cases II and IV) could any intake of alcohol be established. The other 3 patients were more or less confirmed abstainers. Dietary histories were also negative as to providing any possible etiologic clues. Mental deterioration was observed in Case V, in a patient who was quite senile and demonstrated advanced arteriosclerosis. In none of the patients was there any evidence of syphilis. All the patients were males, and this is also in keeping with the reports of Rossi,[6] Marie, Foix and Alajouanine,[7] and Romano, Michael and Merritt.[5]

The encephalographic findings in the 5 cases reported also showed numerous char-

acteristics common to all. The cerebral ventricular systems were uniformly enlarged in 3 cases, this enlargement being most conspicuous in Cases III and V. There was a slight degree of cerebral cortical atrophy in Cases II, III, and V. The cisterna cerebello-medullaris was enlarged in all 5 cases, this being most marked in Cases I, III, and IV. Enlargement of the perichiasmatic and prepontine cisterns was observed in Cases I, II and V while Case IV showed unusually large air pockets in the lateral recesses of the posterior fossa. Besides the increase in the size of the normally present basal posterior fossa cisterns as an indication of reduction in the size of the cerebellum, Case V displayed another encephalographic criterion by which atrophy of the cerebellum might be surmised. This consisted in an outlining of the individual cerebellar folia by subarachnoid air, and the demarcation of the primary and secondary sulci. The presence of the encephalographic picture alone, even without any increase in the size of the posterior fossa cisterns, appears as definitely indicative of extensive cerebellar cortical atrophy.

The presence of encephalographic evidence for cerebellar atrophy in 5 consecutive cases entering the Neurological Service of the Boston City Hospital within a period of nine months renders the inclusion of encephalographic examination of patients with similar disorders as routine procedure almost a necessity. Thus not only would a confirmation of the clinical diagnosis be provided by a rather simple procedure, but in a larger series may help to correlate the clinical symptoms with the gross anatomical changes taking place within the cerebellum itself during the course of the evolution of the disease.

SUMMARY

Five cases of primary cerebellar atrophy are reported. In every one of these patients, all of whom were males of different national extractions, the disease had appeared insidiously after the third decade of life, without any family history of similar neurological affection. In only two of the cases could the use of alcohol be established. There was no evidence whatsoever to indicate that any of the patients had ever had syphilis. Encephalographic studies in every of these five cases supported the clinical diagnosis in demonstrating a reduction in size of the cerebellum in relation to the posterior fossa. This reduction varied in amount from a slight enlargement of the medullo-cerebellar cistern and increased amounts of accumulated air between the cerebellar folia, to the apparent reduction of the cerebellum to almost two-thirds of its normal mass. Considering the relative paucity of cases of primary cerebellar atrophy in the neurological literature, and the dearth of pathological examinations on those cases actually reported, it is suggested that encephalography might prove useful in confirming a diagnosis which, however accurate and well founded, would otherwise lack direct, objective evidence.

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Vol. 60, No. 3

ACCURACY OF ROENTGEN DETERMINATION OF ACTIVITY OF MINIMAL PULMONARY TUBERCULOSIS

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THE photofluorogram has been welcomed as the solution to the two-fold problem of tuberculosis control: finding the infective source for the purpose of isolating it and finding the early case at a stage amenable to therapeutic measures. Its introduction has, however, raised new questions. At the present time ever larger population groups are being surveyed and constantly growing numbers of "positives" are being discovered with the result that sanatorium and hospital facilities threaten soon to be swamped unless criteria which are reliable, yet simple in application, are shortly established as a guide in the disposition of the newly discovered case.

What to do with the patient with extensive tuberculosis of either the exudative or cavitary types is not the concern of this paper. These are diagnostic problems in only the exceptional instance and their disposition is a problem only in relation to available facilities. What to do with the small non-cavitary lesion discovered during mass surveys is a problem which resolves itself into two components: first, the differential diagnosis; second, the disposition of the case once it has been identified as tuberculous.

The question of differential diagnosis is important because of the great number of non-tuberculous, as well as tuberculous, lesions which will be found in a survey program as extensive as that now being developed. This matter has been the subject of some discussion in recent literature and it has been recommended that no one "attempt to diagnose any pulmonary pathologic condition by x-ray" on the ground that the changes "are not pathognomonic."[7] Others have proposed complex and detailed schemes for the differential diagnosis of "abnormal pulmonary findings" because they consider the diagnosis of pulmonary tuberculosis on the basis of roentgen examination alone "scientifically unsound."[3]

There can be no argument against the routine tuberculin testing of all individuals with abnormal chest roentgenograms. A negative skin test is strong evidence that the lesion is not tuberculous. On the other hand, it must be recognized that a positive reaction in no way simplifies the differential diagnosis since it *excludes nothing.* Those who feel that reactors with roentgen findings can then be divided into active and inactive, or even tuberculous and non-tuberculous categories on the basis of sputum examinations or gastric aspirations take too sanguine a view of the problem, in our opinion. In a sense the converse of the remark about the tuberculin test applies to these examinations. While the *unequivocal* demonstration of acid-fast bacilli is diagnostic, negative sputum examinations and gastric aspirations are no great help. Occasional specimens or series of specimens may be negative in an undoubted or proved case with extensive disease (Fig. 1) and this situation is more likely to be encountered in the smaller lesion. Several reports have recently emphasized that positive findings may sometimes be obtained only by repeating gastric aspirations as many as twelve to eighteen times.[4,8]

The proponents of the disposition schemes based on sputum findings themselves state that not all laboratories are qualified to do such examinations and that certified centers must be established to provide this service.[3] Also, unless collected

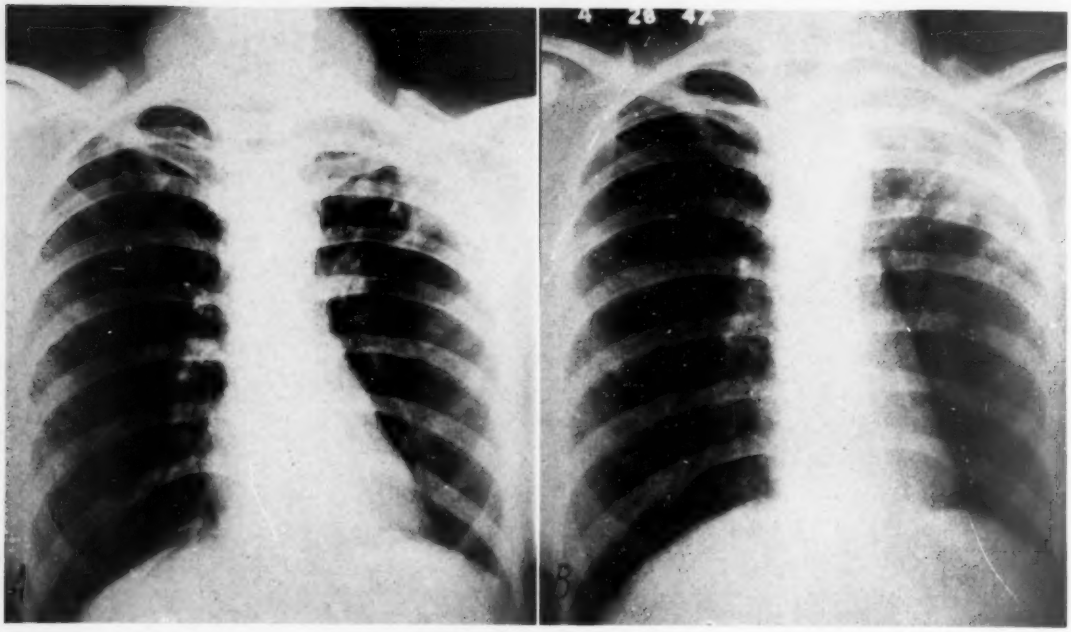

FIG. 1. *A*, active tuberculosis in white female, aged twenty-one, on routine examination. Repeated sputum and gastric examinations negative for four months. *B*, at time streptomycin therapy had begun to prevent irreversible changes. First positive culture reported after streptomycin therapy was initiated.

under some measure of observation there is always the possibility of deliberate substitution of sputums.

Scheduling patients for a number of gastric aspirations presupposes a degree of enlightened cooperation not always encountered in our clinic patients, many of whom are disinclined to return even for follow-up roentgen examinations. In the first five months of 1947, a total of 581 cases of minimal tuberculosis alone were reported by our clinic. Assuming that three successive gastric aspirations would be done on each with negative routine sputums it would be impossible to follow this procedure without a marked increase in staff and facilities.

It has been established that gastric washings deteriorate rapidly and that the percentage of positives obtained drops sharply in the first three days.[9] After seventy-two hours it is no longer worth while to examine such specimens. Where reliable laboratories are not available it would be more feasible to send the roentgenogram to a competent roentgenologist for evaluation than to send sputum or gastric washings. Finally, not the least important shortcoming of the bacteriologic diagnosis of the small pulmonary lesion is the lack of permanently available evidence for restudy and comparison in prolonged follow-up.

It is our purpose to outline the methods employed by the Detroit Department of Health and present an analysis of the results obtained under the difficult conditions encountered during the war years, namely, a shifting industrial population and a shortage of field workers required to maintain an adequate follow-up on diagnosed cases.

METHOD EMPLOYED BY THE DETROIT DEPARTMENT OF HEALTH

Not only is the differential diagnosis made by the roentgenologist but, whenever possible, an opinion as to the activity of the lesion, if tuberculous, is expressed at the time of the initial examination. The disposition, if active, is determined by home conditions and number of beds available

at the time. From the beginning of the period covered in this report to the present time, there has been a substantial number of diagnosed cases in excess of available beds. This, as well as consideration of the social and economic stresses on the families involved, has made it imperative that no facilities be dissipated on any case not definitely active.

1. If the initial roentgenogram is interpreted as showing evidence of an active minimal tuberculosis, that patient should be hospitalized as soon as possible and, if other studies are confirmatory, the therapeutic measures applicable will be employed.

2. If the initial roentgenogram is interpreted by the roentgenologist as showing no evidence of activity but there is evidence of hemoptysis, wheezing, or extrapulmonary tuberculosis the disposition will depend on the clinician's evaluation since the presence of any of these modifies the prognostic value of the roentgenographic findings.

3. If the initial roentgenogram shows an inactive minimal tuberculosis and there are no significant clinical findings, the patient is instructed to return for reexamination in three months. Meanwhile tuberculin and sputum studies should be carried out. The roentgen examination should be repeated at three month intervals for at least two years and thereafter every six months to a year for an indefinite period, possibly the rest of the patient's life. The interval between observations must be shortened and special vigilance will be exercised when hygienic conditions are poor, when the patient is a member of one of the more susceptible racial groups, and during periods of stress such as pregnancy and the period following delivery.

We do not subscribe to the statement that pulmonary roentgen changes are not pathognomonic. Such changes have been described and checked against postmortem findings often enough to establish the roentgen characteristics of tuberculous lesions, and occasions for repeating such correlations continue to arise (Fig. 2). Nor do we entirely agree with the statement recently made that "to attempt to determine the activity of proved tuberculous lesions by a single x-ray shadow is preposterous."[7] Those who have watched far

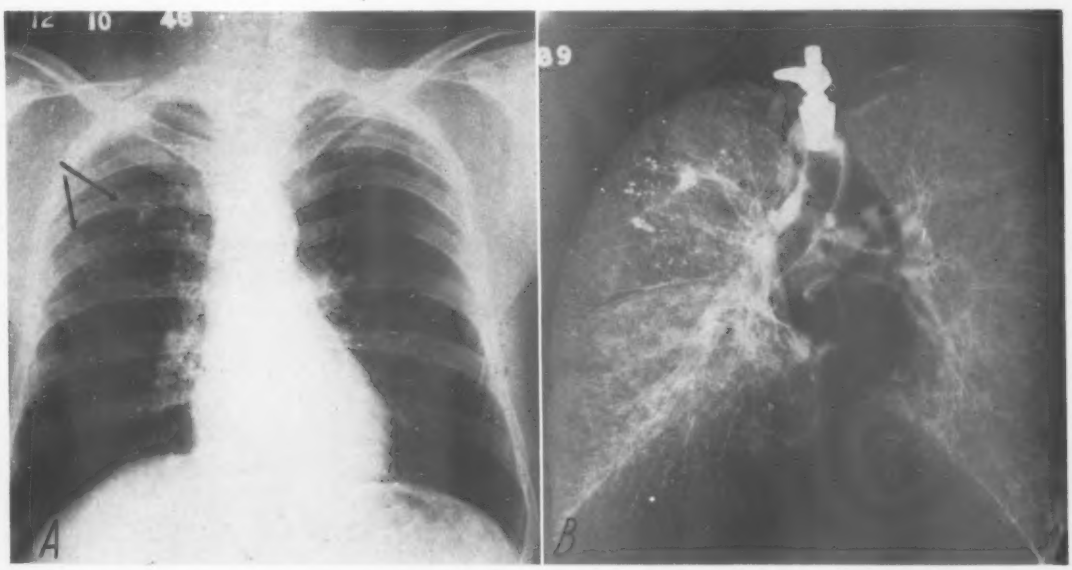

Fig. 2. *A*, White male, aged forty-four. Interpreted as inactive. Treated elsewhere for "tuberculous adenitis" and finally referred back comatose as "tuberculous meningitis." Autopsy revealed lymphosarcoma, generalized, and obsolete pulmonary tuberculous process. *B*, postmortem inflation roentgenogram.

and moderately advanced tuberculosis regress to small stable remnants under therapy (Fig. 3) know that such lesions have characteristics by which they may be recognized, and realize that such regression frequently occurs unobserved in the undiagnosed case. It is our estimate that more than 75 per cent of all *minimal* lesions seen by us in surveys have acquired stability at the time they are first observed. Actually 90 per cent of the 581 cases of minimal tuberculosis reported by this clinic in the first five months of 1947 were interpreted as being inactive, and the estimate of 75 per cent is derived by application of the least favorable correction for diagnostic error possible, based on the findings of this study.

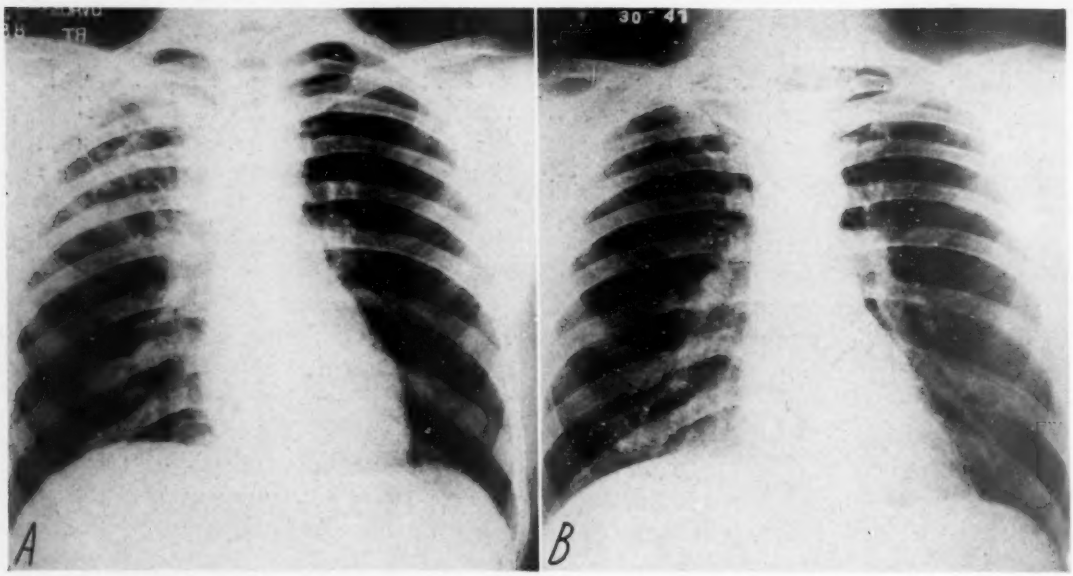

FIG. 3. *A*, active excavating disease in white male, aged twenty-two, in 1934. Pneumothorax for four years. Regressed sufficiently to be acceptable for full duty in Pacific with Armed Forces. *B*, present small remnant.

Perhaps the greatest source of error in the interpretation of the survey roentgenogram is an insufficient appreciation of normal variation coupled with a determination not to overlook the very earliest lesion. It should be remembered that the normal pattern of lung markings varies to as great a degree as other physical characteristics and that some experience beyond that acquired in a short course of film interpretation is required in reading even survey roentgenograms. Some recent surveys have been conducted by interpreters who were not fully qualified radiologists.[6]

The tuberculous lesion in its earliest form is typically a small unilateral soft snowflaky process commonly found in the upper half of either lung (Fig. 4). A little later similar soft shadows may appear on the opposite side but also usually in the upper half. Such lesions may progress and involve extensive areas. If they regress they may diminish in size until they disappear entirely (Fig. 5) but more commonly they leave small nodular or string-like scars (Fig. 2 and 3). Those who have observed this sequence frequently are in a position to express an opinion as to the stability of a given lesion from its appearance on the roentgenogram with a considerable degree of accuracy. This fact is of tremendous value in recognizing a residual or regressive stage which should be identified as such and closely observed but not subjected to immediate treatment or hospitalization.

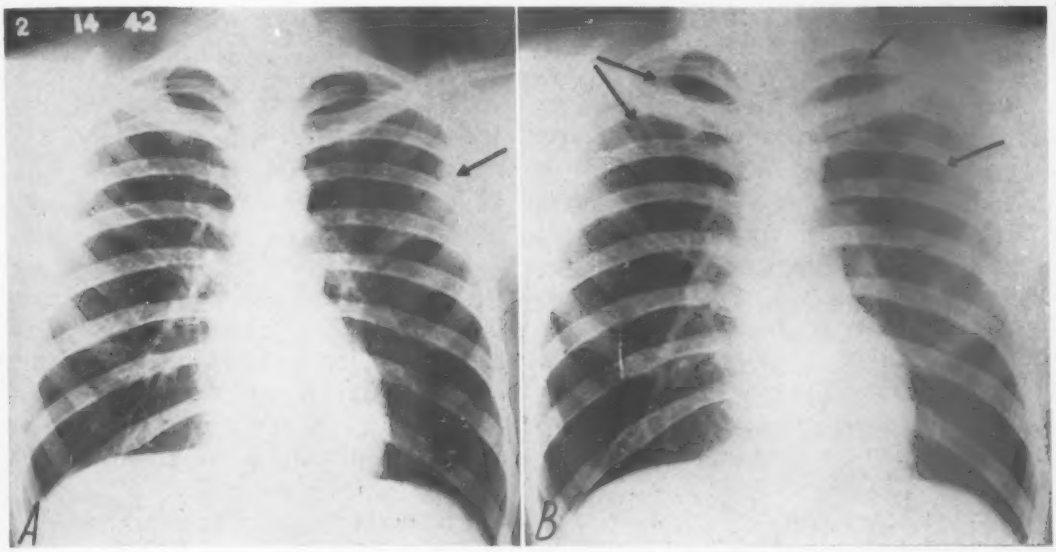

Fig. 4. *A*, fresh exudative lesion left infraclavicular area in white male, aged twenty-four. Refused hospitalization. *B*, extension to both apices.

PLAN OF STUDY

It was decided to study all cases of minimal tuberculosis reported by the Detroit Department of Health in the five year period 1940 to 1944 inclusive. Thus, by definition, the study would be confined to the small, non-cavitary lesions which must be evaluated purely from the quality of the roentgen findings. It was further felt that the two year follow-up period thus possible on even the most recent cases would be adequate to prove or disprove the accuracy of the initial reading. This assumption might seem to be open to question in view of some of the findings.

During this five year period 3,635 cases

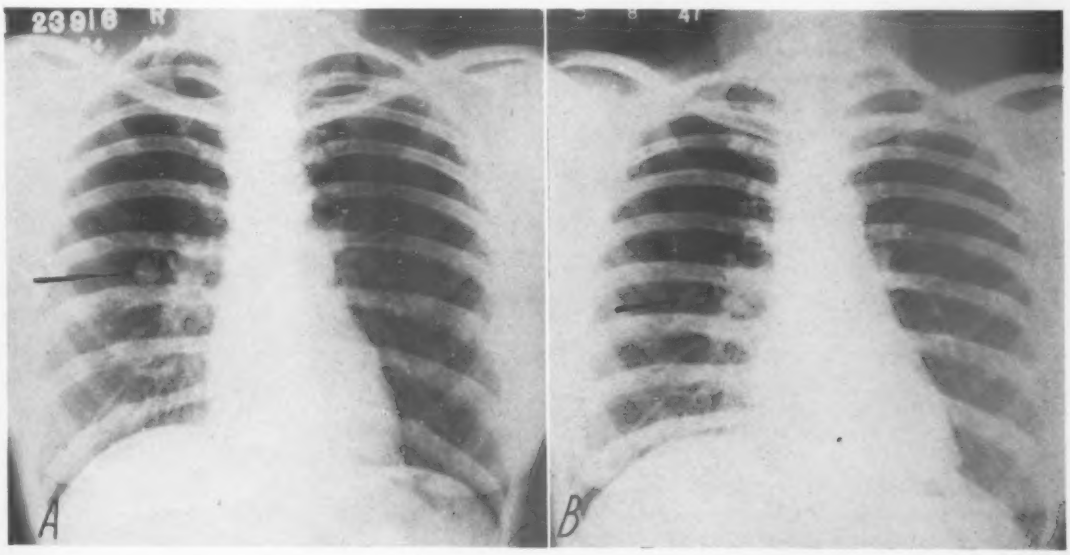

Fig. 5. *A*, white female, aged thirty-six, new lesion at right hilum in 1943. Sputum and gastric examination negative. Lesion has gradually regressed and would not now be visible without prior knowledge of its location and significance, *B*.

of minimal tuberculosis were reported by physicians, hospitals, and industrial concerns in the City of Detroit. Of these 2,557 were roentgenographed by the various units maintained by the Department of Health. However, from a study of the ratio of cases reported inactive to cases reported active for each year it is apparent that inactive minimal tuberculous lesions were not reported as scrupulously at the beginning of this period as in 1944.

	Active	Inactive
1940	119	149
1941	133	134
1942	186	242
1943	173	608
1944	156	657
Total	767	1,790

Only records of cases actually reported were available for study. *However, any previously unreported case which activated* before January 1, 1947, would be picked up as a prognostic error in our statistics. A two year observation period, or observation until activity was demonstrated, was obtained in only 765, one-third of the 2,557 cases initially examined by one of the Health Department units. The analysis of these 765 cases according to the initial interpretation "active," "inactive," or "questionably active" and the final results are shown in Table 1.

CRITERIA OF ACTIVITY

A lesion was considered to have demonstrated activity if there was evidence of any of the following during the period of observation:

1. *Change in the roentgen appearance of the lesion*, applying the dictum "a changing lesion is an active one." On this basis a clearing lesion is considered active, the only permissible exception being a gradual contraction, over a period of years, of a definitely fibroid process. Four of the "errors" (cases originally called inactive but later showing activity) had never been hospitalized and never had positive sputum reported but did show roentgen evidence of change.

2. *Positive sputum.* Two cases were listed as errors because of positive sputum or culture although no therapeutic measures other than bed rest were ever applied and there was never any change in the roentgen appearance of the lesion.

3. *Hospitalization*, unless the discharge note definitely stated that such observation definitely confirmed the original impression of inactivity.

4. *Therapeutic procedures*, other than bed

TABLE I

RESULTS OF TWO YEAR FOLLOW-UP OF 765 MINIMAL TUBERCULOUS LESIONS

	Reported Minimal Inactive			Reported Minimal Active			Reported Minimal Questionably Active		
Year	Number	Showed no Activity	Showed Activity	Number	Showed no Activity	Showed Activity	Number	Showed no Activity	Showed Activity
1940	55	43	12	21	2	19	4	1	3
1941	88	74	14	21	3	18	15	0	15
1942	99	90	9	29	4	25	16	2	14
1943	157	128	29	38	3	35	21	4	17
1944	173	154	19	18	1	17	10	1	9
Total	572	489	83	127	13	114	66	8	58
Active	14.5%			Active	89.75%		Active	88.0%	
Accuracy	88.5%			Accuracy	89.75%				

Total accuracy of interpretation, active and inactive 86.43%

rest alone, regardless of the indications since it would be impossible to prove that the eventual favorable outcome was not due to collapse measures. Three patients are carried as errors because they received ambulatory pneumothorax elsewhere. It was impossible to ascertain whether any of them had positive sputa or any other evidence of activity prior to collapse.

5. *Death of the patient*—unless evidence was available that tuberculosis played no part in the death. Any patient diagnosed as having tuberculosis in any stage who later develops some other illness and dies is likely to be reported as having died of some complication of tuberculosis. Figure 2 shows roentgenograms of a patient who entered the hospital in a moribund state with a presumptive diagnosis of tuberculous meningitis and died in a few days. This would have been carried as one of the errors had not an autopsy been obtained which established the diagnosis of lymphosarcoma. On the other hand, in those cases which died at home the cause of death had to be accepted as reported even though it might be some improbable combination such as "sunstroke and tuberculous meningitis" reported in one instance.

ANALYSIS OF RESULTS

Sixty-six cases were interpreted as being questionably active on the first examination. These were mostly lesions in which the character or quality of the infiltration did not justify a definite opinion as to stability. A few were of the type referred to as "coin lesions." They have been previously described[2] and when first seen must be regarded with suspicion (Fig. 5). A very few were listed in the questionable category simply because an opinion as to stability had been omitted through oversight or because only a small film (4 by 5 inch) or a technically imperfect film was available and opinion was deferred pending re-examination for which the patient failed to return. Of these 66 cases, 58 (88 per cent) eventually showed some evidence of activity.

Among the remaining 699 cases on whom definite opinions as to stability had been expressed the follow-up substantiated the original interpretation in 604, or 86.43 per cent. The apparently greater accuracy of

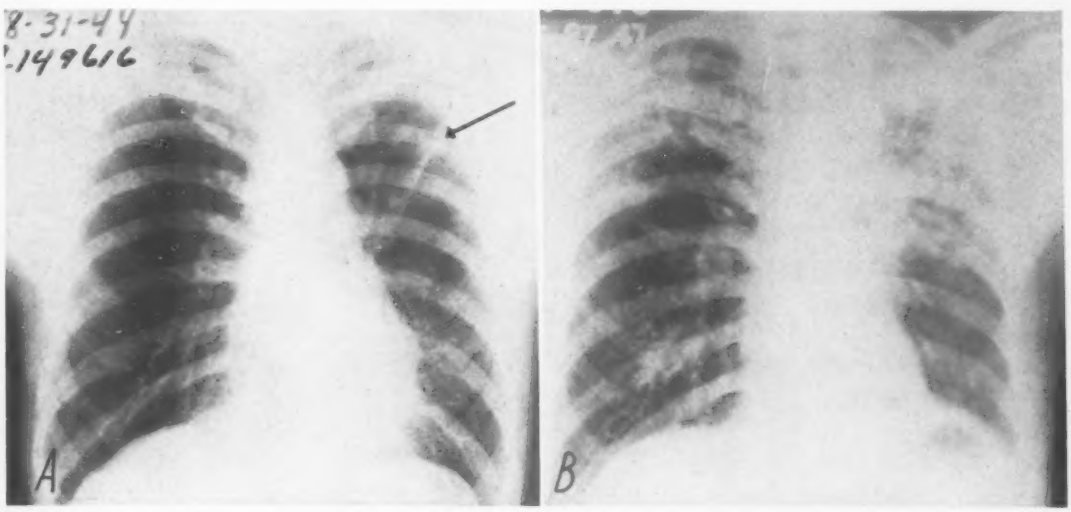

Fig. 6. *A*, photofluorogram of Filipino male, aged forty-one, read minimal inactive in 1944. Refused to return for re-examination. Consulted private physician in May, 1947, who referred him to one of our survey units. *B*, now has far-advanced tuberculosis.

TABLE II-A

Year	Number	Lost through Obsolete Address	Failed to Cooperate	Evidence of Activity	No Activity	Other
1940	27	9	17	—	—	1*
1941	38	23	14	—	1	—
1944	235	50	134	2	48	1†
Total	300	82	165	2	49	2
	Total recovered for re-examination				51	
	Recovered cases showing activity				2	
	Active 4%	Accuracy 96.0%				

* Died of cancer of throat.
† One case serving in Korea; probably inactive, but not included among inactives.

prediction of 89.75 per cent (114 proved active) among the 127 read active as opposed to 85.5 per cent (489 remaining inactive) among those 572 read inactive is partly due to the greater tendency for return of the active cases. When these break down and become symptomatic they tend to be referred back by their physicians or to return of their own accord (Fig. 6) or when incidental roentgen examination elsewhere discloses extension of the pulmonary process this information is reported to us and the case then appears as an "error" on these statistics. On the other hand, the individual whose first few check-up roentgenograms show no extension often considers it too troublesome to continue his return visits and is therefore lost to us. If all such cases could be re-examined regularly the degree of accuracy would, in our opinion, be significantly improved in the group read inactive on first examination. Conversely, the percentage of error might be greater in the group originally called active.

TABLE II-B

EFFECT OF SPECIAL FOLLOW-UP STUDY ON PERCENTAGE OF ACCURACY

	Number	Accuracy
1. 1944 inactive group		
(a) original	123	85.4%
(b) final	173	89.1%
2. Total 5 year group		
(a) original	714	85.4%
(b) final	765	86.4%

Some indication of the results obtainable with better control of the patient is shown by a study of 1,592 employees called inactive tuberculosis from roentgenographic findings and approved for work with a large industrial corporation during the years 1942–1946.[5] These cases were available for re-examination at intervals as designated by the roentgenologist. The incidence of activation was 1.38 per cent which implies a prognostic accuracy of 98.62 per cent.

From an administrative point of view it was impossible to recall all of our 1,791 cases on whom a two year study was not obtained. However, a sample of 300 cases initially interpreted as "minimal inactive" was selected (on no other basis than that their period of observation had been less than one year) and an effort was made by letter to persuade these people to return for another roentgen examination. It was hoped that one-third (100 cases) might respond and the results might, by inference, shed some light on what happens to lost cases. However, the response, as indicated in Table II-A, was disappointing. Of 65 cases first examined in 1940 and 1941, 32 were lost because of obsolete addresses as indicated by unclaimed letters. Thirty-one apparently received letters but did not cooperate. One had died of carcinoma of the larynx and only one came in for a roentgen examination, which showed that the lesion had not changed. Of 235 letters sent to

patients first examined in 1944, 50 were returned because of obsolete addresses. One hundred thirty-four patients received letters but did not cooperate. Fifty returned for roentgen examinations. Of these, 48 showed no change at the time of re-examination and 2 showed evidence of activity. Poor as this response was, it sufficed to change the percentage of accuracy for 1944 alone from 85.4 per cent to 89.1 per cent, although the percentage of accuracy of prediction for the entire five year inactive group is not altered significantly, the change being only 1.03 per cent (85.4 per cent to 86.43 per cent. Table II-B). If one were permitted to project the findings in this small series of recalled cases for the entire group of 1,791 lost cases, a final over-all prognostic accuracy of 90 per cent or better might be anticipated.

It might be well at this point to anticipate the objection that the results obtained could in part be due to overreading insignificant lesions among which the breakdown rate would naturally be low. Without exhibiting all 572 cases read inactive this is difficult to refute since it is known that the correlation of opinions of different interpreters reading the same films is not absolute.[1] For this reason, we analyzed all cases referred to the clinic in 1944 with roentgen diagnoses of minimal tuberculosis made elsewhere. Our interpretations of roentgenograms on these patients were as follows:

Our Interpretation	Number	Per Cent
Minimal	5	4.2
Minimal inactive	62	52.1
Fibrosis Calcium deposits No evidence of tuberculosis	52	43.7
	119	100

As indicated, 43.7 per cent of these 119 cases had been interpreted in this Department as showing no evidence of tuberculosis. This would seem to indicate that the results obtained are not due to overreading.

ERRORS IN DETERMINING ACTIVITY

It was hoped that from the standpoint of improving future accuracy an analysis of the 83 "mistakes" among the cases originally called inactive might yield useful information and a better understanding of the roentgen-ray quality of an unstable lesion. This was not the case. In 4 instances it was felt that the initial reading had been

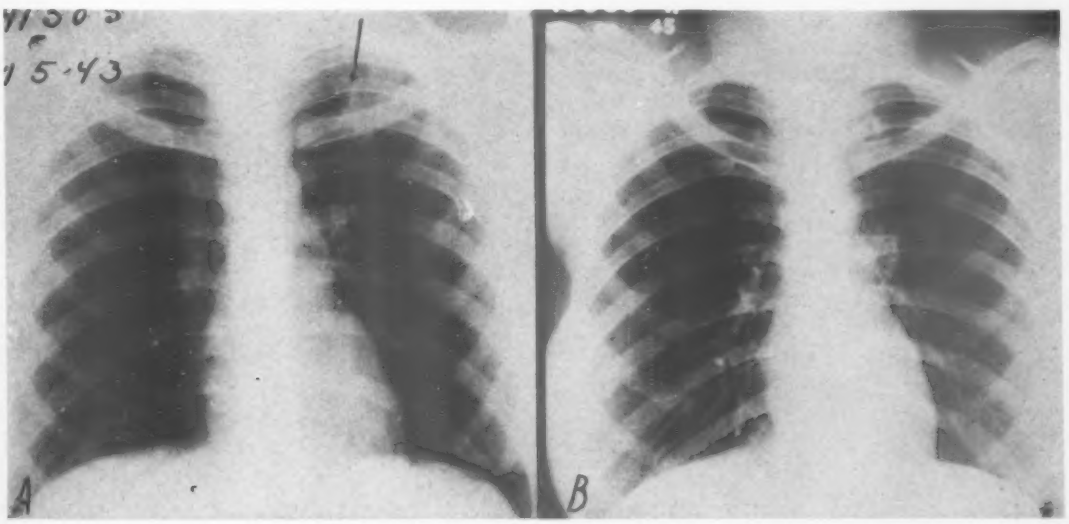

Fig. 7. *A*, colored female, aged eighteen, in 1943. Showed only gradual contraction of process for two years. *B*, at time of delivery in 1945. Early re-examination advised at this time but patient failed to return. Died elsewhere of far-advanced pulmonary tuberculosis.

incautious. In 2 more it was felt that error resulted from attempting to determine activity from the small (4 by 5 inch) film (Fig. 6). Despite reports to the contrary[1] we do not believe that the 4 by 5 inch film is as reliable as the 14 by 17 inch, and, although at times forced to interpret activity from the photofluorogram because of film shortages during and after the war, we believe its use should normally be confined to screening. A diagnosis should be made only from the 14 by 17 inch film.

In the remaining 77 cases it was felt that without knowing the final outcome, the initial roentgenogram would still be read as "inactive." Of these, 4 spread coincident with pregnancy; 2 in less than a year, 1 after one year, 1 after two years (Fig. 7). Another spread following tracheotomy for carcinoma of the larynx. On many records the statement appeared that the patient was an alcoholic, or uncooperative. However, the difficulty in getting follow-up roentgenograms on all of these patients indicates that lack of cooperation is not characteristic of the "breakdown" group alone.

The analysis of the "errors" according to the period of apparent inactivity and present status is summarized below:

Group I Less than 1 year inactivity			48	57.8%
A. Hospitalized at once		8		
B. No follow-up films prior to "breakdown"		18		
C. Activity evident on 1st routine check-up x-ray		13		
D. Less than 1 year inactivity on routine check-ups		9		
Total Group I		48		
Group II Less than 2 years but more than 1 year			15	18.1%
Group III Less than 3 years but more than 2 years			12	14.5%
Group IV Less than 4 years but more than 3 years			7	8.4%
Group V One 5 years			1	1.2%
Total			83	100 %
Less than 2 years	63	76%		
More than 2 years	20	24%		
Total	83	100%		

Eight cases were hospitalized at once despite a roentgen interpretation of inactive pulmonary tuberculosis. This is properly an important part of the program. If there is evidence of hemoptysis, tracheobronchial disease, or extrapulmonary tuberculosis, the clinician will hospitalize the patient regardless of the roentgen interpretation. Eighteen cases had no follow-up roentgenograms between the initial reading and the time activity was demonstrable. In 1 case there was a five year lapse following the first roentgenogram; when the patient did return his disease was far advanced. Such cases were considered to have no proved period of stability. Thirteen cases showed change on the first routine re-examination and therefore had no proved periods of stability. In 9 cases routine check-ups showed no change for periods of several months but less than one year. These four categories, totaling 48 cases (57.8 per cent) comprise Group 1, those with less than one year of apparent stability. Group II includes 15 cases (18.1 per cent) with more than twelve months but less than two years of apparent inactivity as demonstrated by periodic re-examination. Group III, 12 cases (14.5 per cent) two or more years' stability. Group IV, 7 cases (8.4 per cent) three or more years. One case (1 per cent) was followed five years before there was roentgen evidence of activity. Thus it is seen that 20 cases (24 per cent) of the "errors" broke down some time after the second year of observation which again raises the point, alluded to in the beginning of this paper, that a lesion

which has demonstrated apparent inactivity for two or more years is not necessarily a "safe" lesion and that roentgen follow-up at regular intervals must be continued for an indefinite period.

It would be fruitless to speculate here on the question of reinfection versus reactivation. In only one of these cases did the "spread" definitely appear to involve a new lung area while the original lesion remained unchanged. It should be unnecessary to point out that it is not in any sense implied that a lesion is "sterile" when it is called "inactive."

The present status of cases showing activity originally read inactive can be summarized as follows:

Deaths	18
Hospitalized at present	16
Apparently arrested	36
Status not known	13
Total	83

The 18 deaths were all assumed to be due to tuberculosis. This includes the case which spread following tracheotomy for laryngeal carcinoma. According to available information, 16 patients are in sanatoriums at the present time. Thirty-six cases are apparently arrested. The present status of 13 cases cannot be determined. These are individuals who left the city or otherwise concealed their whereabouts after leaving the hospital against advice or upon being informed that their disease had become active.

An analysis as to age, race, and sex of the 83 errors compared with proved inactives, as well as the entire 11,062 cases of adult or reinfection type tuberculosis of all stages reported for this same-five-year period from the City of Detroit, was attempted.

The error group is too small to be of great statistical significance, but it would appear that the younger patient is more likely to have an unstable lesion. This is to be expected as the younger patient has the more recent infection. An anticipated higher degree of stability of minimal tuberculous lesions among white persons as compared to non-white persons could not be demonstrated. This is perhaps due to the small number of cases.

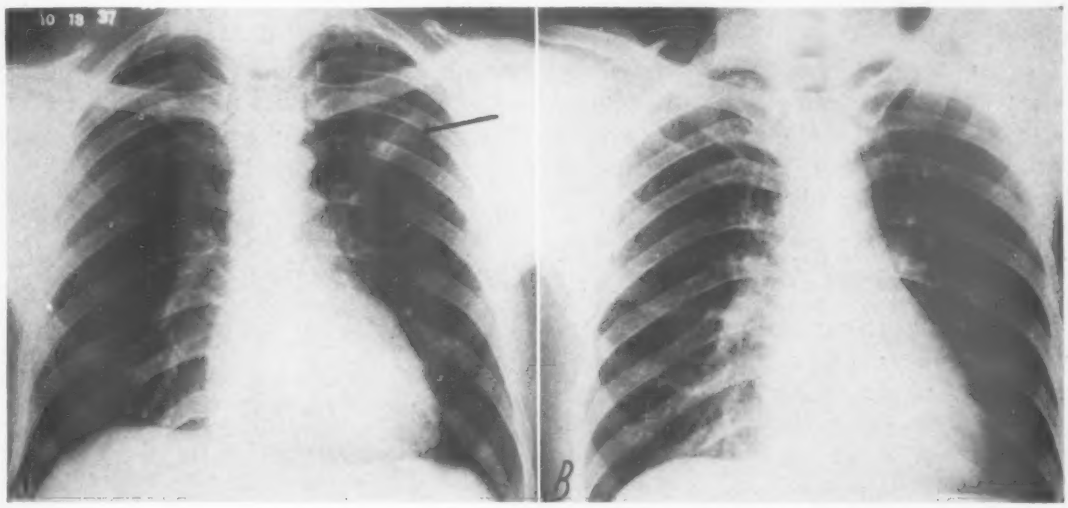

Fig. 8. *A*, white male, aged thirty-three, with history of exposure and positive tuberculin test. No symptoms. Read active minimal tuberculosis. *B*, complete clearing in two weeks.

Errors in Differential Diagnosis

One case interpreted originally as minimal inactive tuberculosis proved eventually to be primary carcinoma of the lung. It

must be pointed out that in this case, a colored male, aged twenty-eight, the disposition would have been the same on the basis of tuberculin test, which was positive, sputum studies, and gastric aspirations. Some confusion resulted from a false positive sputum report. The lesion was still inaccessible to the bronchoscope when its true nature was first suspected. A correct diagnosis could only have been made by examining bronchial secretions for malignant cells, a method not then widely used. Thoracotomy was done, but the lesion was not resectable.

One would anticipate that the pneumonias, particularly of the virus or atypical variety, would be the greatest source of error in the differential diagnosis. Although this error has occurred and will no doubt continue to occur in this clinic (Fig. 8) there were no examples in this particular series due to the method of selecting material; only reported cases of minimal tuberculosis were included in the study. When the possibility of confusing tuberculosis and pneumonia exists, the reporting is delayed until the diagnosis can be clarified. It is the policy of this Department to recommend re-examination in four weeks when a pneumonia is suspected whereas re-examinations are requested at three month intervals if the initial diagnosis is inactive minimal tuberculosis.

CONCLUSIONS

1. As a result of mass surveys increasing numbers of minimal tuberculous lesions are being discovered. More than 75 per cent of these have acquired stability at the time they are found.

2. It is important, particularly in large metropolitan areas, that a rapid and accurate estimate of activity be made to permit a concentration of effort on the active case and avoid dissipation of facilities on the inactive case.

3. Activity can be determined accurately by roentgen examination and more rapidly and economically than by bacteriologic methods. In a group of 699 cases of minimal tuberculosis followed for two to five years, activity was correctly determined from the first roentgenogram in 86.43 per cent.

4. Success in such a program depends on the services of an experienced roentgenologist and the use of the large film.

5. The photofluorogram should be used for screening only.

6. Patients with minimal inactive pulmonary tuberculosis should be followed by roentgen examinations at three month intervals for two years from the time of discovery and at longer intervals for an indefinite period thereafter.

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Vol. 60, No. 3

TUBERCULOSIS OF THE STOMACH AND DUODENUM*

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GASTRIC and duodenal tuberculosis are uncommon lesions. Proof, following operation or autopsy on a patient who was considered to have benign ulcer or carcinoma, usually causes considerable surprise to the physician. There are certain suggestive findings in the roentgen examination which, while not conclusive, may lead to the correct preoperative or antemortem diagnosis. These we intend to discuss.

INCIDENCE

The largest series was reported by Good[10] in 1931. He found the average incidence of gastric tuberculosis in autopsies and gastric resections from the Mayo Clinic and other published figures to be 0.34 per cent. If only the cases with other tuberculosis were considered, the incidence rose to 1.4 per cent. Other series have shown a much lower incidence: Hardt and Cohen[12] found 1 case in 1,000 autopsies of tuberculous patients. Windwer[26] reported 1 case in 21,000 hospital admissions. There were 3 cases in Cook County Hospital from 1929 to 1938 (Sullivan *et al.*[21]). There has been a total of 10 cases at the Mayo Clinic up to 1943 (White[24]).

Duodenal tuberculosis is much rarer. Migliaccio[15] states that there are only 12 proved cases limited to the duodenum and regional lymph nodes up to 1946. However, about 10 per cent of gastric tuberculosis has associated duodenal involvement, and when the pylorus is involved the incidence of duodenal lesions is very high (Ricard and Chevrier[20]).

At the Philadelphia General Hospital there have been 2 cases of gastric and 1 case of duodenal tuberculosis since 1936.

PATHOGENESIS

Many authors (Broders,[3] Renander,[19] White[24]) have discussed the probable routes of infection. The possibilities are: (1) direct infection through the mucosa; (2) through the blood stream; (3) by lymphatic channels; (4) spread by continuity from adjacent structures, especially the lymph nodes. There is no reason to suspect that all may not operate at different times, but in a number of cases the involvement of adjacent mesenteric nodes seemed the primary lesion. This will be discussed later.

The reason for the rarity of gastric and duodenal tuberculosis when the disease is so common to the rest of the gastrointestinal tract is obscure. Suggested elements have been: (1) the gastric acidity; (2) presence of an intact mucosa; (3) scarcity of lymphoid structures in the gastric wall; (4) the rapid emptying time of the stomach; (5) inherent resistance. None of these have been proved.

TYPE OF LESIONS

Gastric. The commonest lesion, which occurs in about 80 per cent of cases (Broders[3]), is the ulcer. This may be single or multiple, large or small, and usually occurs on the lesser curvature side between the incisura and the pylorus. The other major type is the proliferative or hypertrophic, in which there is invasion of the gastric wall and very often tumor formation. The tumor frequently causes an annular constricting lesion very much like carcinoma (Broders,[3] Good,[10] Browne[4]). There is often a combination of ulcer and tumor or ulcer and infiltration. Other types which are less important are solitary or miliary tubercles, larger nodular foci, and diffuse tuberculous gastritis. All usually have extensive lymph node involvement which may dominate the picture (Ackermann[1]).

Duodenal. The hypertrophic type particularly may extend through the pylorus and involve the duodenum (Matthews,[14] Cames[5]). Single or multiple ulcers are

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found in the duodenum which often lead to considerable deformity (Reeves[17]). The second and third portions are involved much more frequently than in the usual peptic ulcer (Cames,[5] Grossman,[11] Migliaccio[15]). Perforation, sinus tracts and fistulae may occur (Psenner,[16] Wichtl,[25] Beresford-Jones[2]).

Associated Lesions. The commonest associated lesion is tuberculosis elsewhere in the body. Isolated gastric and duodenal tuberculosis, however, does occur. Good[10] states that at operation tuberculosis of the stomach is met with just as frequently in subjects in whom no other tuberculosis can be demonstrated. About 10 per cent of the cases in the literature have associated gastric carcinoma (White[24]). Enlarged mesenteric and retroperitoneal tuberculous lymph nodes are a prominent finding in almost all recorded cases.

ROENTGENOLOGIC FINDINGS

Most authors have found nothing characteristic in the ulcerations or hypertrophic lesions demonstrated roentgenologically. The appearance is that of carcinoma or benign ulcer and, in the case of pyloric lesions, the preoperative diagnosis usually has been carcinoma or syphilis. Renander[18,19] calls attention to a hypertrophic polypoid appearance of the involved mucosa. In one of his cases he found an hour-glass constriction of the pars media which was felt to be more rounded and cuff-like than the usual appearance. He also notes a relative lack of interference with peristalsis in what appears to be an extensive carcinoma. Ackermann[1] noticed this finding and also demonstrated a sinus tract extending from the duodenal cap. He points out that involvement of the duodenum as well as the stomach is a suggestive diagostic point.

CLINICAL ASPECTS

The symptoms are not characteristic. There is usually pain after meals, loss of weight and strength, and vomiting (Good,[10] Walters,[22] *et al.*). Fifty per cent have a palpable mass (Walters[22]). The treatment is radical surgical resection. Prognosis is good when the lesion is isolated and otherwise depends on the extent of tuberculosis elsewhere (Good[10]).

REPORT OF CASES

CASE 1. M. McG. The patient was a white woman, aged forty-five, born in Ireland. She was first admitted to the hospital on the service of Dr. T. Klein, September 7, 1943, complaining of enlargement and breakdown of nodes. The onset of her disease had been five or six years before with enlargement of the cervical lymph nodes. Some of these opened spontaneously and others were incised by her physician, resulting in a number of draining sinuses. Several years later other nodes in the axilla, breast and inguinal region appeared, as well as nodules in the soft tissues of her arms. There were occasional bouts of chills and fever, some anorexia and weight loss.

On physical examination she was emaciate[1] and showed generalized adenopathy. There were scars in the submaxillary region from previous sinuses. Multiple masses were palpated in the abdomen and nodules were present in both upper arms. Biopsy of an axillary lymph node was reported as showing a large area of caseation surrounded by epithelioid and giant cells and many small tubercles. The diagnosis was tuberculosis of lymph node (Dr. W. E. Ehrich). Roentgen examination showed the chest to be essentially normal except for some moderate elevation of the right diaphragm. There was no evidence of calcification or abnormal masses in the abdomen.

The patient was discharged from the hospital on September 16, 1943. As an out-patient she received roentgen therapy to the cervical, axillary and inguinal regions On February 9, 1944, she was readmitted because of chills and fever, night sweats and loss of weight. For the last two months she had had nausea but no vomiting. Gastrointestinal roentgen examination on February 18 (Fig. 1, 2 and 3) showed a large ulcer on the lesser curvature of the pars media with some induration of the adjacent gastric wall. No peristalsis passed through the region of the pyloric antrum, which appeared rigid and infiltrated. There was marked alteration in the normal mucosal markings in the antrum as well as in the pars media. The pylorus was eccentric and there was 40 per cent gastric retention in twenty-four hours. No

abnormality was noted in the duodenum. Roentgen examination of the chest was essentially normal.

The patient developed epigastric pain which became worse in spite of a Sippy regimen. Sputum smears and cultures for the tubercle bacillus were negative on numerous occasions. Gastric washings were also negative. The blood Wassermann and Kline reactions were negative. The blood showed a mild anemia and leukocytosis. Gastric analysis revealed free acid of 39 per cent and a total of 53 per cent, with a faint trace of blood. On April 19 laparotomy was performed by the service of Dr. W. E. Burnett. There was heavy infiltration serosally extending upward to the cardia from the lower third of the lesser curvature Around the stomach and in the mesentery there were many lymph nodes suggestive of widespread tuberculosis adenitis. The stomach was opened and two ulcers resembling benign peptic ulcers were seen. The stomach was then closed and resected, which was difficult because of many adhesions A perforation pocket with abscess formation was opened on the lesser curvature and 3 to 5 cc. of contents removed.

Pathological Report. Gross description by Dr. E. Mertens: "The specimen is the lower 13 cm. of the stomach. The serosal surface shows a sinus opening near the pyloric end. There are adhesions about this, and a thickened, indurated area which occurs at the upper extremity of the specimen. Several nodes are included. The largest measures 1.4 cm. and shows caseation on section. The mucosal surface shows a soft cobblestone roughening everywhere. There are multiple ulcers, some shallow and hemorrhagic and others shallow and necrotic. There is one with a crater measuring 1.5 by 1.0 cm. on the lesser curvature at the upper end of the specimen. Another, with a much hypertrophied edge showing extensive undermining, leads to the sinus opening near the pyloric end. There is also a small opening on the lesser curvature at the upper end, leading to the excision line. Impression: Gastric tuberculosis with multiple ulcers and fistula."

Microscopic examination by Dr. W. E. Ehrich: "Several sections through ulcers, fistulous tracts and lymph nodes all show the characteristic picture of tuberculosis with epithelioid cells, Langhans' giant cells and caseation necrosis. There is nothing to suggest malignancy here. *Pathological diagnosis:* Tuberculosis of stomach."

FIG. 1. Case 1. Gastric tuberculosis. Large, penetrating ulcer on lesser curvature of pars media, with surrounding infiltration of gastric wall. There is gastric dilatation from partial obstruction at the outlet, due to the associated involvement of the pyloric region.

The patient did well following operation and was discharged on May 29. On August 7, 1944, she was readmitted in extremis with a history of vomiting, abdominal pain, swelling of the abdomen, loss of weight and diarrhea. She died two days later. Only a limited autopsy was done. Extensive miliary tuberculosis of the abdominal organs with tuberculous peritonitis was found. There was no gross evidence of pulmonary tuberculosis.

CASE II. I. H. The patient was a colored male, aged twenty-five, who was admitted to the service of Dr. D. Spotts on October 21, 1945 with a chief complaint of hematemesis. His history went back to 1943 when he had an acute attack of vomiting and low abdominal pain of short duration. In 1944 there was vague abdominal pain followed by occasional vomiting. The pain, at first only at night, later appeared following meals, and for the last week he had vomited blood on several occasions. He now had sharp pain in the abdomen radiating toward the chest. There was a 20 lb. weight

loss during the last three months. Physical examination revealed adbominal distention with tenderness on the right side and some enlarged inguinal lymph nodes. Initially there was a mild anemia which became more severe during the period of hospitalization. Gastric analysis disclosed a free acid of 32 per cent and a total of 81 per cent. The blood Kline reaction was negative.

Roentgen examination on November 9, 1945 (Fig. 4), showed a dilated, atonic stomach with obstruction at the pylorus or the first portion of the duodenum. The duodenum was not well visualized during the examination. Lung fields were normal.

Laparotomy was performed on November 20, 1945, by Dr. P. A. McCarthy. A dilated and very large stomach was found. There was a large duodenal ulcer with massive surrounding adhesions. Gastric resection at the upper third with gastroenterostomy was done. The surgical diagnosis was duodenal ulcer.

Postoperatively the patient did not do well and a fistula developed in the wound. A sub-

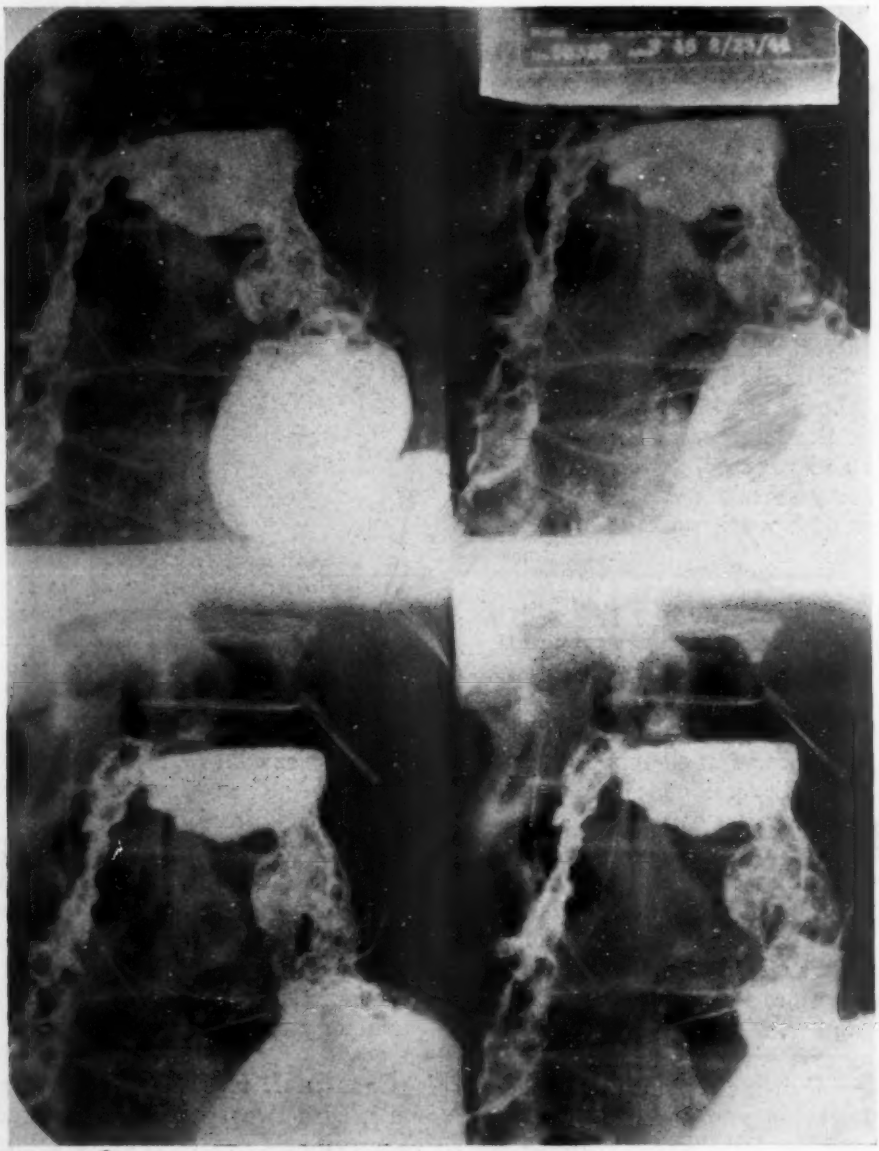

FIG. 2. Case 1. Gastric tuberculosis. Deformity and rigidity of prepyloric region. Loss of normal mucosal folds.

diaphragmatic abscess was suspected clinically and by roentgen examination. There was spiking fever and the patient weakened progressively and died on January 12, 1946.

Autopsy by Dr. A. Valdes-Dapena: "*Gross examination:* Practically all the nodes of the lymph nodes and adhesions. The mucosa shows a peculiar appearance: it is studded with light gray nodules about 2 mm. in diameter; these are soft and some of them can be squeezed out, yielding a light yellow paste. This condition prevails from the proximal stump for at least

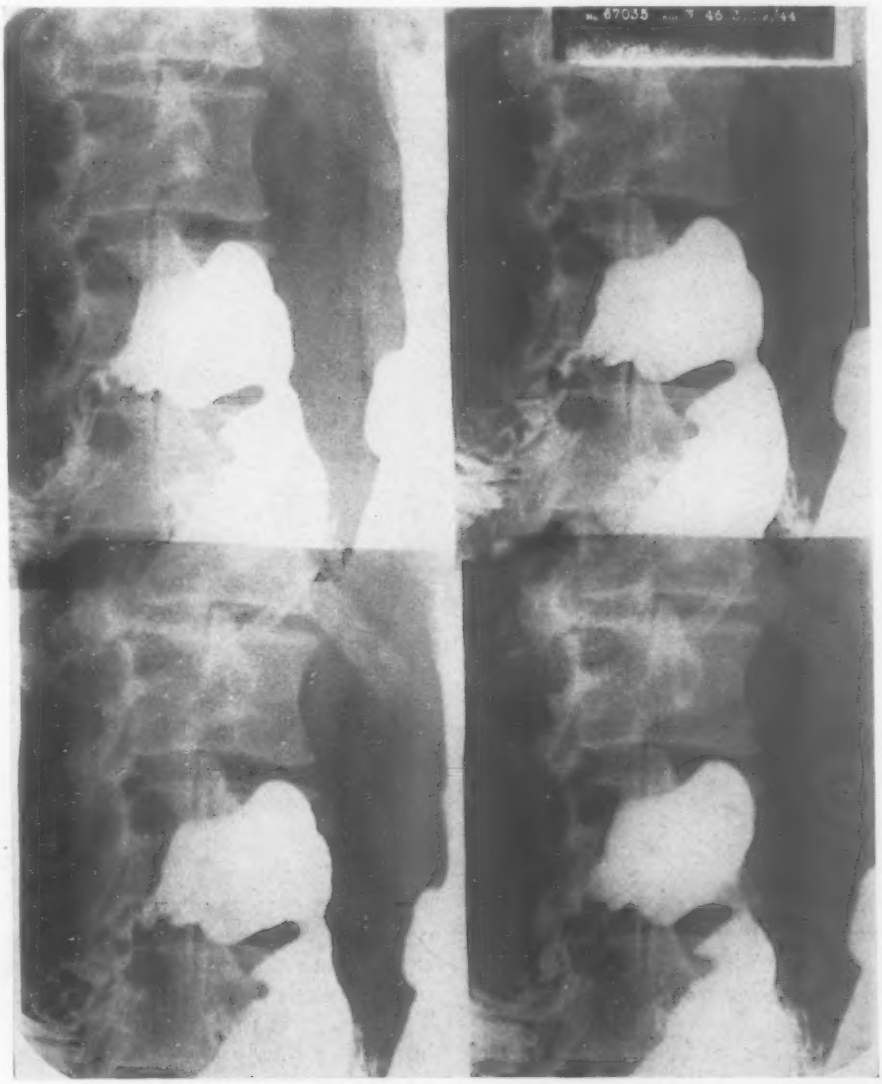

FIG. 3. Case 1. Gastric tuberculosis. Further deformity of prepyloric region, six weeks after Figure 2. The pylorus is eccentric. The lesser curvature ulcer is also seen.

peritoneal cavity are enlarged. The largest measures 2 to 3 cm. in diameter. The nodes around the hilum of the liver are matted together and adhere to the surrounding structures especially to the duodenum. Masses of nodes surround the common bile duct and the pancreas. The duodenum is surrounded by matted 10 cm. down the duodenum. There are several small ulcers, some of them appearing to communicate with the suprahepatic space. The liver is located in the midst of adhesions. To the left there is a cavity limited on one side by the liver and on the other by the diaphragm. This cavity contains what seem to be food material

and a yellowish paste. The cavity communicates through a long tract with a small opening in the upper part of the wound. It also appears to have communicated with one of the small ulcers in the duodenal stump.

"*Microscopic examination:* Sections taken from the abdominal lymph nodes show caseation necrosis due to tuberculosis. There is tuberculous infiltration of the duodenum. Lungs: marked passive congestion; acute parenchymatous degeneration.

"*Final diagnosis:* Tuberculosis of abdominal lymph nodes and duodenum with perforation."

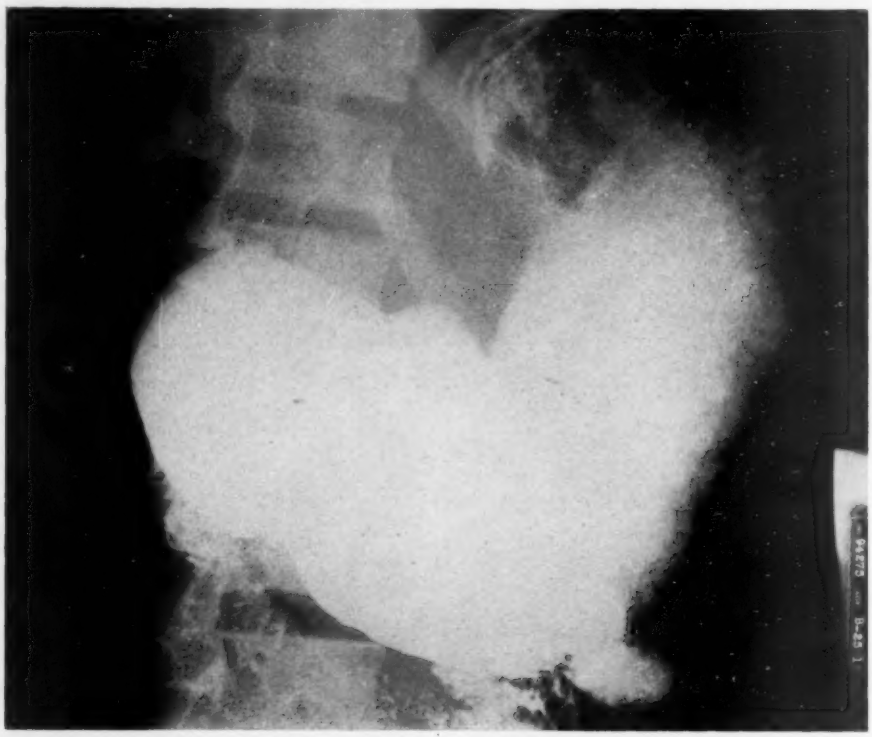

FIG. 4. Case II. Duodenal tuberculosis. Grossly dilated stomach, the result of obstruction in the duodenum.

CASE III. S. A. The patient was a colored male, aged forty-three, admitted to Philadelphia General Hospital August 13, 1943, on the service of Dr. C. Brown. The patient had had loss of weight and occasional abdominal pain since early in the year. At the out-patient department of another hospital, a gastrointestinal series and gastric analysis were negative and the only abdominal finding was hepatomegaly. Since May there had been vomiting and loss of weight and strength. On admission he was emaciated and the liver and spleen were much enlarged. Laboratory studies showed the gastric free acid to be 49 per cent and total acid 98 per cent. There was a positive reaction for occult blood. The red blood cell count was 3,000,000 with anisocytosis, poikilocytosis, and macrocytosis. The white blood cells were not increased. The blood Kline reaction was positive. Sputum was negative for tubercle bacilli. A roentgenogram of the chest on August 26, 1943 was negative except for elevation of the right diaphragm, and film of the abdomen showed an enlarged liver with some distention of the bowels and thickening of the segments. The patient was treated conservatively and was improving slowly when he died suddenly on September 16, 1943.

Autopsy by Dr. D. R. Coman: "*Gross examination:* The esophagus is negative. The stomach contains 1,500 cc. of fresh blood. There is a large peptic ulcer on the lesser curvature midway between the esophagus and pylorus, measuring 5 cm.; its base presents a gaping artery. Two and a half centimeters above this ulcer there is another ulcer with a dirty, granular base, and from it a fistulous tract leads through masses of fibrous tissue to an abscess

in the lesser peritoneal cavity. A part of the fistula runs beneath the peptic ulcer. Near the latter are two smaller ulcers. The small intestine, especially the jejunum and ileum, presents large, thick, granular patches; the serosal surfaces over these lesions are studded with tiny tubercles.

"The liver and spleen are enlarged and show many caseous nodules. Mesenteric, peripancreatic and perigastric nodes are enlarged to three or four times normal size, and on section reveal caseation necrosis. The lungs show only a calcified nodule 2 to 3 mm. in diameter and one calcified mediastinal node. There is also some calcification and fibrosis in the pleura on the right.

"*Gross diagnosis:* Tuberculous ulcer with fistula of the stomach. Peptic ulcer with eroded artery. Tuberculous abscess, lesser peritoneal cavity. Hyperplastic tuberculosis of the small intestine. Caseous tuberculosis of the liver and spleen. Healed primary tuberculosis of the lung.

"*Microscopic examination:* There is caseous tuberculosis of the liver and spleen. The stomach shows caseous tuberculous gastritis with ulceration."

DISCUSSION

Pathologically the chief characteristic of all 3 patients was the presence of multiple ulcerations and fistulous tracts. A perforation pocket with abscess formation was present on the lesser gastric curvature in Case I, as well as a sinus near the pylorus. In Case II there was a perforation of the duodenum and a tract leading to a subdiaphragmatic abscess. Case III had a tract from a gastric ulcer to an abscess in the lesser peritoneal cavity. Although we did not demonstrate these tracts roentgenographically, similar findings have been shown before (Psenner,[16] Wichtl,[25] Ackermann[1]). If such sinuses or fistulae can be demonstrated, a tuberculous etiology should be strongly suspected.

Other roentgenologically suggestive findings are simultaneous involvement of both the stomach and duodenum by the disease, which was not present in our cases. In Case I the large lesser curvature ulcer, extensive mucosal changes and infiltration of the pylorus might have suggested tuberculosis, but a malignant condition could produce the same appearance. Gastric tuberculosis was suspected in this woman because of the known tuberculosis of lymph nodes. Case II showed nothing roentgenographically except obstruction at the outlet of the stomach; the duodenal perforation probably occurred at a later date.

The extensive involvement of the surrounding lymph nodes in all cases is interesting. The lymphatic disease may even be the primary lesion. Certainly in Case I the patient had recognized tuberculosis of lymph nodes for years before the development of gastric symptoms. A similar case, reported from the Massachusetts General Hospital,[6] also had peripheral tuberculous adenopathy for years before development of duodenal tuberculosis with subsequent perforation. There had been no evidence of ulceration or mucosal changes in the duodenum two months before death, but there was deformity of the third portion due to pressure of an extrinsic mass, evidently a lymph node. In our Case II also it was the pathologist's opinion that the duodenal infiltration was secondary to the lymph node disease.

None of our patients had evidence of active pulmonary tuberculosis, and at autopsy only a calcified primary complex was found in one of them. The absence of a pulmonary lesion should not be considered evidence against gastroduodenal tuberculosis.

SUMMARY

1. Two cases of tuberculosis of the stomach and one of the duodenum are described. In all three cases the lungs showed no active pulmonary tuberculosis. One patient had had peripheral tuberculous adenitis for years, and in all three cases abdominal lymph node involvement was a very prominent feature. All three patients developed perforations or fistulous tracts at the site of their lesions.

2. From the roentgenologic standpoint there are no pathognomonic findings. The ulcerative and infiltrative lesions can

easily be confused with benign ulcer or carcinoma. A combination of both types of lesions, as well as extensive mucosal nodularity, as in one of our cases, might be suggestive. The most significant findings that can be demonstrated roentgenographically are simultaneous involvement of the stomach and duodenum, the presence of fistulae or sinuses, and signs of external pressure by enlarged lymph nodes. These should make the examiner strongly consider the likelihood of tuberculosis, even in the absence of any pulmonary lesion.

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TUMORS OF THE UPPER THIRD OF THE STOMACH*

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WHEN speaking of the upper third of the stomach we understand it to be the fundus proper, the cardia and the portion situated immediately beneath it. We include also in this paper tumors of the abdominal esophagus, believing it is justified by the frequency of invasion observed in both parts, whichever one may be the primary site of the growth. Very rarely are the tumors discovered when they are confined to their initial location. The tumors that make up this group require special mention, as the anatomic conditions peculiar to the region give them unique features and explain in certain measure how they can be more easily overlooked than tumors of the middle and lower thirds.

The upper third of the stomach is situated deep in the left hypochondrium and is inaccessible to palpation under the screen. Another difficulty encountered in the diagnosis of lesions located here is the fact that the opaque substance, when the examination is made in the vertical position, passes rapidly through this part without stopping, and in the routine examinations in the Trendelenburg position the abundant quantity of barium that spreads hides them unless they are marginal or have reached considerable size. Apart from this, the growths at this level are not so frequent and the roentgenologist has a tendency to examine this area less carefully than the other regions.

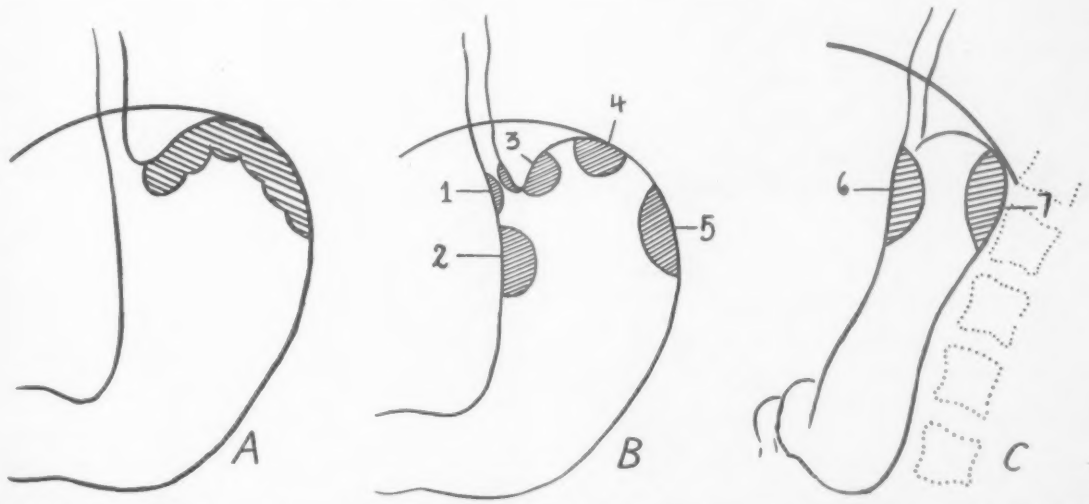

FIG. 1. Different locations of tumors of the upper third of the stomach. *A*, massive, *B*, *1*, tumor of the cardia; *2*, tumor of the lesser curvature immediately beneath the cardia; *3*, tumor of the medial margin above the cardia; *4*, tumor of the superior margin; *5*, tumor of the lateral margin; *C*, *6*, tumor of the anterior surface; *7*, tumor of the posterior surface.

The circumstance that favors the discovery of tumors of this part is the existence of the air bubble of the stomach. In its space the tumor is projected as a soft tissue shadow that alters its outline. When the air bubble does not exist or its shape and size are unusual, the radiologist can exaggerate it by injecting gas. This can be done by the method he prefers (giving mixtures that produce gas or by indirect insufflation through a tube).

Notwithstanding their great value, the

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FIG. 2. Tumor that invades the fornix in massive form. The masses show against the air bubble as shadows of soft part density. (Confirmed by surgery.)

FIG. 3. Stricture of the abdominal esophagus through infiltration. The tumor mass is visible at the medial margin of the fornix. (Confirmed by surgery.)

soft tissue shadows that can be observed in the air bubble may lead to error; because of this it is absolutely necessary to proceed with the method of ingestion of an opaque substance to confirm the diagnosis.

The tumor growths located in the upper third of the stomach often alter the esophagus, the stream of barium entering the stomach, and produce filling defects of

FIG. 4. A neoplasm that infiltrates and ulcerates the abdominal esophagus. Tumor shadow on the medial portion of the fornix.

different localization. As these alterations are conditioned by their location, it is justifiable to separate the following topographic types (Fig. 1, *A*, *B*, *C*):

(*a*) Massive, in which the invasion of the upper third is total.
(*b*) Tumors of the cardia and abdominal esophagus.
(*c*) Tumors of the medial margin of the roof above the cardia.
(*d*) Tumors of the upper part of the lesser curvature, immediately below the cardia.

(*e*) Tumors of the upper surface.
(*f*) Tumors of anterior and posterior surfaces.
(*g*) Tumors of the lateral margin.

(*a*) *Massive forms* (Fig. 2). The massive forms are generally easy to diagnose, as by occupying all or the major part of the upper third they are clearly visible to direct examination, and in supine position with opaque substance.

(*b*) *Tumors of the Cardia and Abdominal Esophagus* (Fig. 3 and 4). These tumors show, as their most notable feature, an obstruction to the passage of the opaque substance, with dilatation of the esophagus. The straight part is seen as a narrow channel frequently ulcerated and of irregular borders. Frequently the shadow of the tumor that invades the gastric roof can be seen.

(*c*) *Tumors of the Medial Margin above the Cardia*. This is the most frequent location of tumors of the upper third of the stomach. They are seen as shadows of soft tissues at this level and frequently deviate

Fig. 5. A tumor situated on the medial margin of the fornix over the cardia that displaces the lower part of the esophagus. (Confirmed by surgery.) The tumor mass is visible in the air bubble.

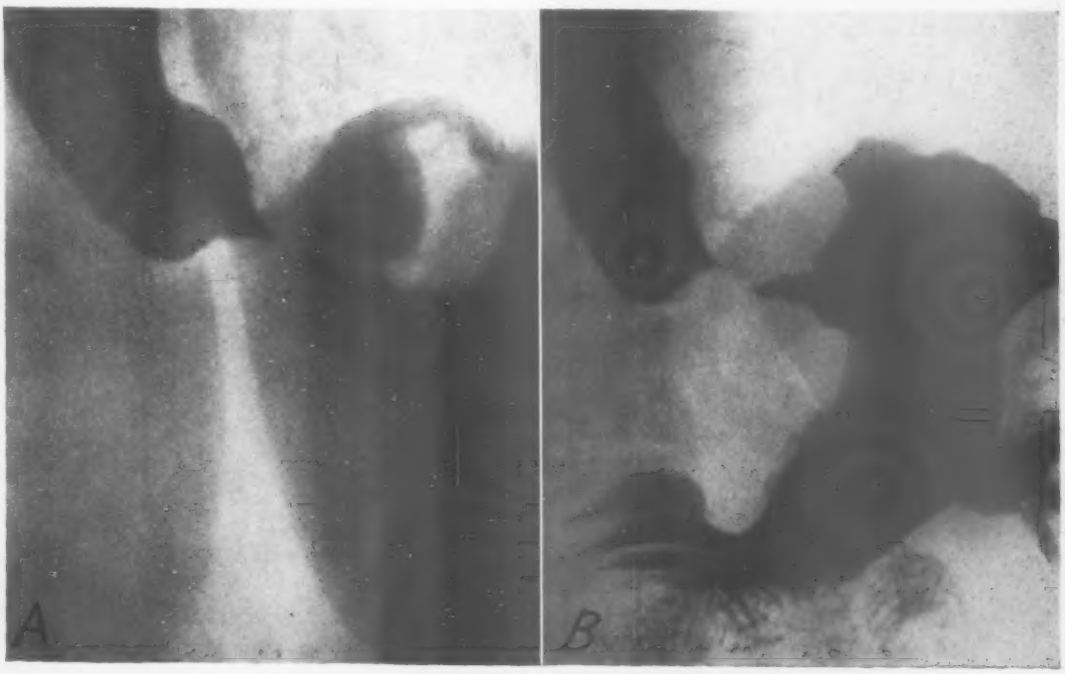

Fig. 6. *A*, a tumor of the medial margin of the fornix, above the cardia; it invades and compresses the abdominal esophagus. Its shadow can be seen in the air bubble. (Confirmed by surgery.) *B*, supine position. Filling defect in the tumor zone.

FIG. 7. Tumor situated at the upper part of the lesser curvature below the opening of the esophagus. The barium column that reaches the stomach is deviated upward by the tumor mass. (Confirmed by surgery.)

FIG. 8. The tumor mass divides the barium column into smaller streams. (Confirmed by surgery.)

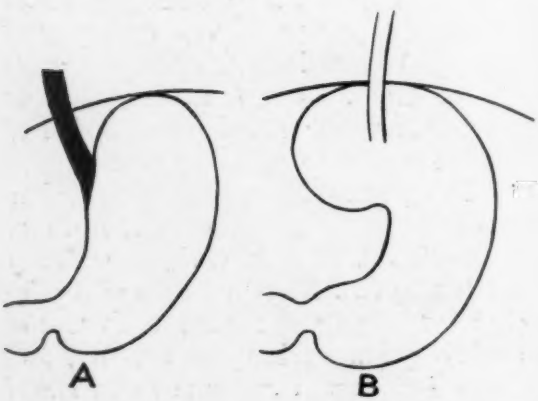

FIG. 9. *A*, the air bubble is of normal size. The study of the esophagus is possible because the air bubble is not superimposed. *B*, the air bubble is distended and superimposes its shadow on the esophagus.

FIG. 10. Tumor of the upper border of the fornix. It deforms the dome of the diaphragm and increases the distance that separates the air bubble from the lung area. (Confirmed.)

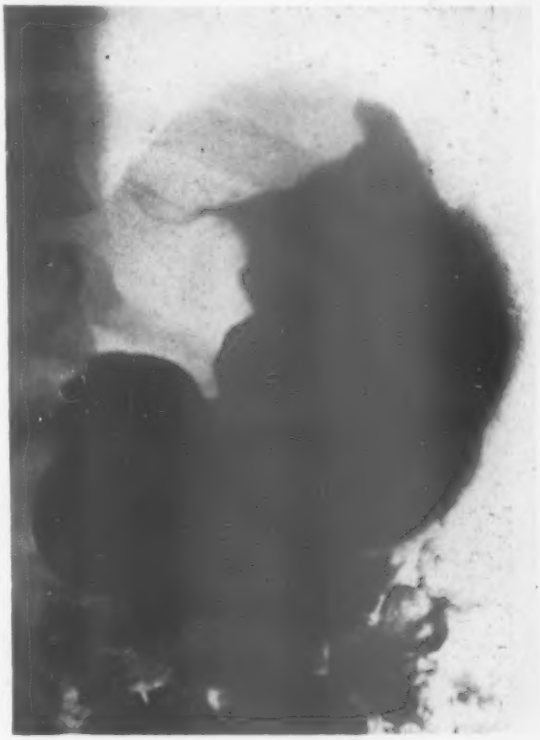

Fig. 11. Tumor of the upper margin of the roof. A filling defect that corresponds to the tumor mass. The supine position is useful in this case because the tumor is marginal. (Confirmed.)

or press upon the abdominal esophagus that runs medial to them (Fig. 5). An examination with opaque medium, in supine position, either horizontal or in Trendelenburg, easily makes them evident (Fig. 6, *A*, *B*).

(*d*) *Tumors of the Upper Part of the Lesser Curvature Immediately below the Cardia.* These tumors either cause deviation of the opaque column that under normal conditions descends by the magenstrasse (Fig. 7), or they interrupt the flow of barium that enters the stomach, dividing it and forming small streams (Fig. 8). These segmentations of the barium column are projections of the tumor mass that obstructs the free flow of the ingested material. Normally the esophageal flow enters the

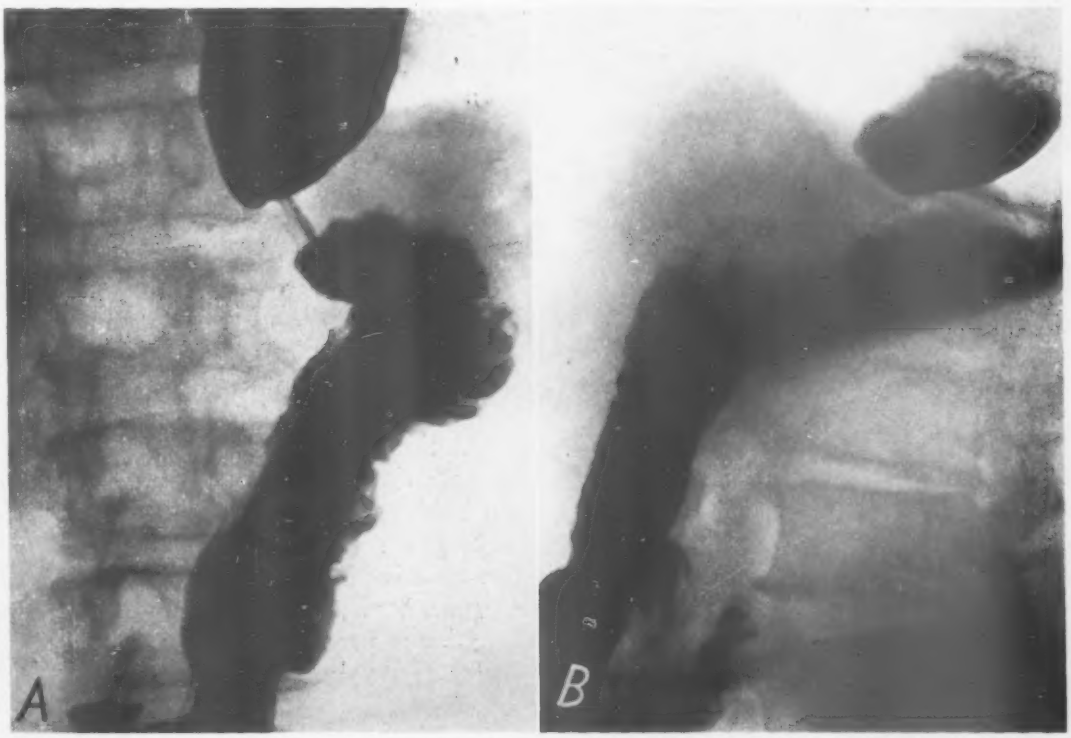

Fig. 12. Tumor of the anterior surface of the fornix. *A*, supine. Invasion of the esophagus by tumor. No typical filling defect is observed at the roof level. It must be remembered that the anterior surface is not marginal in this position. *B*, study in lateral Trendelenburg position; by showing the surfaces it accurately locates the tumor mass on the anterior surface. The filling defect at this level is evident. (Confirmed.)

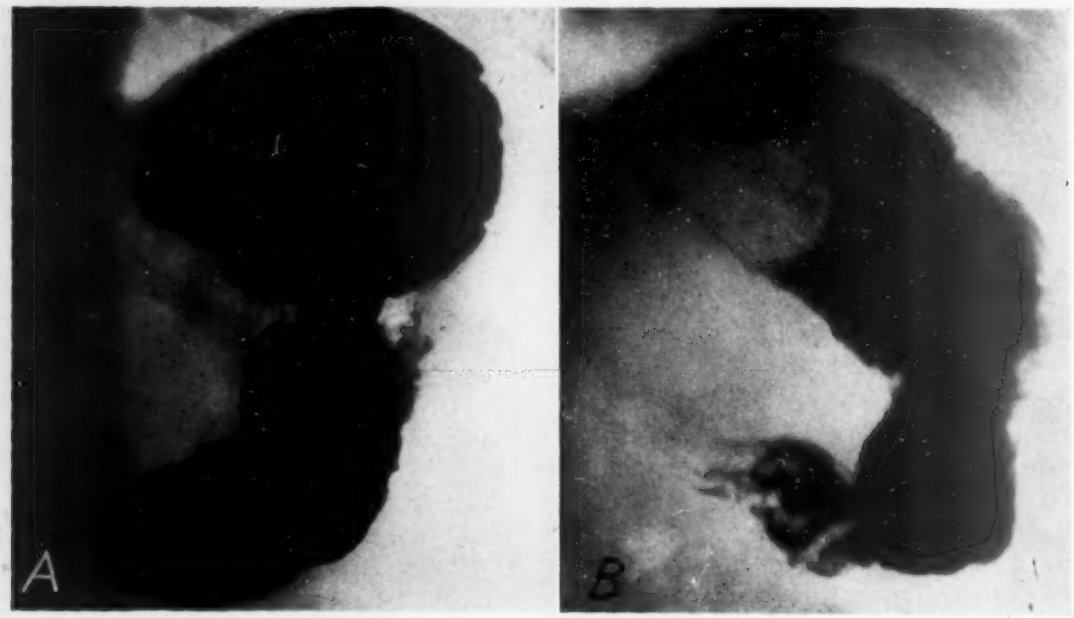

FIG. 13. Submucous tumor located on the highest part of the posterior surface. *A*, studied in Trendelenburg position. In this case the great size of the tumor allows it to be seen in the central part of the fornix. This position is not very useful for tumors that do not invade the lateral, medial or superior margins of the roof. *B*, the study is made in the lateral Trendelenburg position; by showing the surfaces it makes evident the location of the tumor on the posterior surface, with wide parietal implantation and an ulcer in its central part. (Leiomyoma.)

stomach without suffering any deviation and follows the lesser curvature the length of the magenstrasse (Fig. 9).

(*e*) *Tumors of the Upper Surface.* The tumors that develop on the upper surface of the fornix are, generally speaking, evident at direct examination, as their shadows are projected upon the lesser density of the pulmonary background and the transparency of the air bubble (Fig. 10). Also, in the case of these tumors the opaque substance in dorsal decubitus outlines the filling defect that the tumor mass produces, if it has reached a sufficient stage of development (Fig. 11).

(*f*) *Tumors of the Anterior and Posterior Surfaces.* In addition to the soft part shadows that these tumors give against the air bubble, they also produce filling defects of the barium mixture. However, because of their location they are not visible in supine position unless a very small portion of opaque substance is used. This is understandable as they are not marginal in this position and the barium covers them if their volume is not very great. In the Trendelenburg position in lateral decubitus, they are evident as marginal filling defects (Fig. 12, *A*, *B*, and 13, *A*, *B*).

(*g*) *Tumors of the Lateral Margin.* The tumors that arise in this site produce filling defects when the patient is examined in supine position. This is due to the fact that they are marginal in this position (Fig. 14).

DIFFERENTIAL DIAGNOSIS

As the tumors we have studied are seen as soft tissue shadows projected upon the air bubble and as filling defects of the opaque substance, the diagnosis must be made after taking into account all causes, normal or pathologic, intrinsic or extrinsic, that are capable of producing similar images.

(1) Normal elements at the upper third level which may produce false tumor images.

(*a*) Neighboring organs, such as the liver, heart, spleen, and so forth, may super-

impose their shadows upon the air bubble, in the anteroposterior view, making soft tissue shadows similar to those of the tumor. In the case where only a superposition of shadows exists, there is no filling defect when the examination is made with opaque substance. Also, the superimposed image is generally typical of the organ and its location; thus the liver is seen as a shadow at the inner third of the air bubble; the spleen at the outer third and the heart point is seen at the upper portion and changes with the respiratory movements.

(*b*) When the air bubble of the stomach is not properly distended, the folds of the walls may project shadows that give false tumor images; these disappear when the air bubble is filled by insufflation and remain unchanged if the shadows belong to true tumors.

(*c*) It has been said that a thickening of the shadow that separates the roof of the stomach from the diaphragm is a sign of tumor of this area. Although this is a sign often seen in cases of tumor it is not to be solely relied upon, as it may induce error, since this thickness may vary under various circumstances. It is greater when the air bubble is not fully distended. Also, when there is an interposition of parts of the liver or spleen between the roof of the stomach and the diaphragm and at other times, even through an optical illusion of increased distance in the anteroposterior image, when the superior margin of the stomach roof does not coincide with the highest point of the dome of the diaphragm.

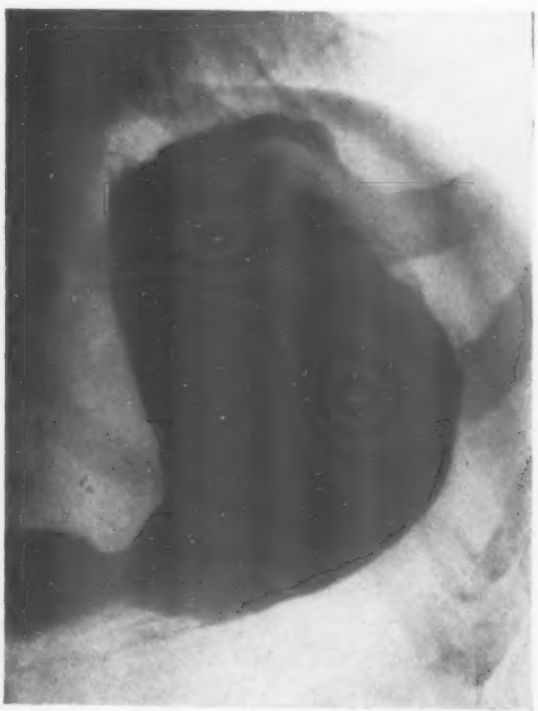

Fig. 14. Tumor of the lateral margin of the fornix. The examination in Trendelenburg position shows the filling defect clearly because the tumor is marginal in that position.

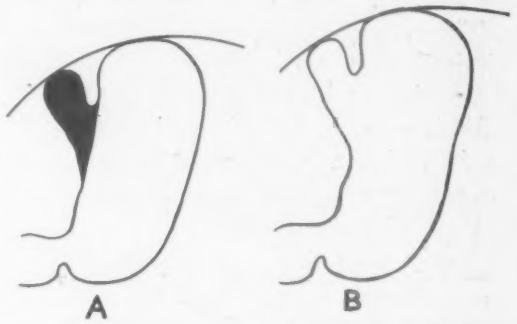

Fig. 15. When the cardia is patent, an examination of the standing patient shows the air bubble and the abdominal esophagus simultaneously filled with air; they are separated by a soft part shadow (incisura cardiaca) that can simulate a tumor. In *A* is seen the aspect of the gastric roof alone when the cardia is firmly closed. The abdominal esophagus (which has been marked in black) does not appear under these conditions. In *B* the cardia is patent and the abdominal esophagus fills with air.

(*d*) A jutting of the esophageal mucosa at the height of the cardia may produce a soft part shadow and defects of filling capable of simulating a tumor (Hodges, Snead and Berger[3]). It is similar to the phenomenon which is sometimes observed in the cecum at the level of the ileocecal valve.

(*e*) In the rare case of a widely open cardia, when the examination is made with the patient standing, both the air bubble and the abdominal esophagus fill simultaneously with gas. These then appear as separated by a soft tissue shadow that drops tongue-like from the roof of the stomach, which could be taken for a tumor

(incisura cardiaca) (Fig. 15). The inner part of the wedge is the terminal portion of the left side of the esophagus and the outer part is the initial portion of the greater curvature at the stomach roof level (Bársony).

(2) Voluminous mucous folds may produce filling defects of tumor-like character. The roentgen diagnosis in these cases is limited to the discovery of the filling defects without its being possible to establish their nature. In this respect Hinkel's case, in which a microscopic investigation was necessary to establish the non-tumor nature, is very illustrative.

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Vol. 60, No. 3

HYDATID DISEASE AND ITS ROENTGEN PICTURE

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ON EXAMINING a great number of patients with echinococcosis, one of the most striking features of the disease is the great variability of the clinical picture, which depends on the localization, vitality and evolution of the primitive parasite, the local complications by infection and rupture and, finally, on the existence and number of metastatic cysts in other parts of the body. This great variability restricts our possibilities of attaining full knowledge of the subject, especially as a great number of cysts cannot be visualized, obliging us to limit our description to those cases which we have seen roentgenologically.

Most authors who have written about *Echinococcus* refer to the high incidence of liver localizations, the percentage being between 55 and 65 per cent of the total, next the lung, with an incidence of 17 to 24 per cent. The remaining cases are divided among other organs, in order of frequency, particularly the bones, kidney and spleen, but practically any organ may be involved.

We have studied 120 cases distributed in the above mentioned order, to which we add for completeness some roentgenograms, which we owe to the kindness of Professor B. N. Calcagno, taken from the 350 cases the latter has seen at the Muñiz Hospital in Buenos Aires over a period of many years.

ECHINOCOCCUS CYSTS OF THE LIVER

For greater clarity and simplicity we propose the following classification of echinococcus cysts of the liver.

(1) Unruptured echinococcus cysts
  (a) calcified
  (b) non-calcified
(2) Infected echinococcus cysts
(3) Ruptured echinococcus cysts emptying
  (a) through the diaphragm into the bronchial tree
  (b) through the biliary ducts to the duodenum
  (c) into the digestive tract
  (d) into the peritoneal cavity (abdominal cysts)
  (e) through the skin (transcutaneous)

The liver cyst becomes calcified more often than the others and is therefore easily visualized. According to the site of the cyst and the extension of the calcification the appearance varies strikingly. The cyst can be completely calcified, being round or oval, with a more or less distinct outline; at other times only a reticulum of wide or narrow meshes can be seen (Fig. 1 and 2). The fact that only one solitary calcified cyst is visible does not exclude the possibility of the presence of other non-visible cysts. Calcification does not imply the biological death of the parasite nor freedom from a subsequent infection and its consequences; on the contrary, they tend to become infected very frequently. We have never seen, during many years of practice, an enlargement of the calcified cyst, a fact that denies the growth of such structures. Frequently several calcified cysts are visible (Fig. 3). The fact that we have never noted calcified intrahepatic structures of any other nature allows us to affirm that the existence of a round reticulated shadow in

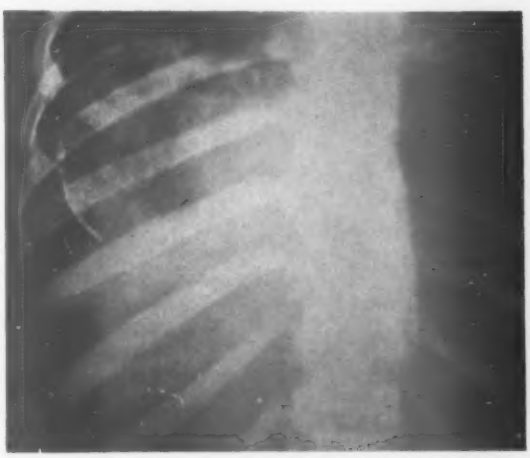


FIG. 1. Hydatid cyst of the liver partly calcified.

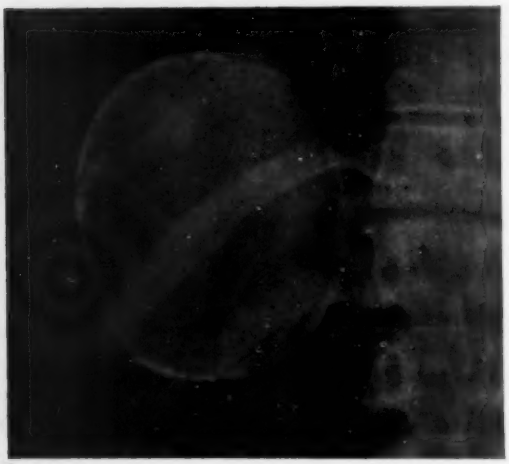


FIG. 2. Hydatid cyst of the liver completely calcified.

the liver is almost pathognomonic of hydatidosis.

The roentgenological difficulties arise in the diagnosis of those cysts with only a slight calcification of the capsule, appearing in the roentgenogram in the shape of fine round or oval lines (Fig. 4 and 5).

All livers containing echinococcus cysts are increased in size, the right hemidiaphragm is elevated, its excursion is impaired and it is divided into two or more arches. This latter is not exclusively characteristic of the disease and can be found more often in other diseases or even in normal conditions. Nevertheless, in endemic regions, round shadows, situated on the surface of the liver, deforming the diaphragm to a great extent point to hydatid disease (Fig. 6 and 16). Occasionally neo-

FIG. 4. Large hydatid cysts of the liver with partly calcified membrane.

FIG. 3. Several hydatid cysts of the liver calcified.

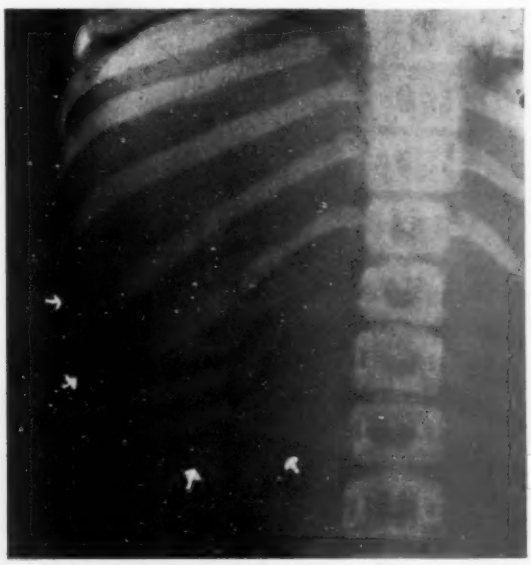


FIG. 5. Fine lines of calcification in the membrane of a large hydatid cyst of the liver.

plastic metastases to the liver show similar pictures.

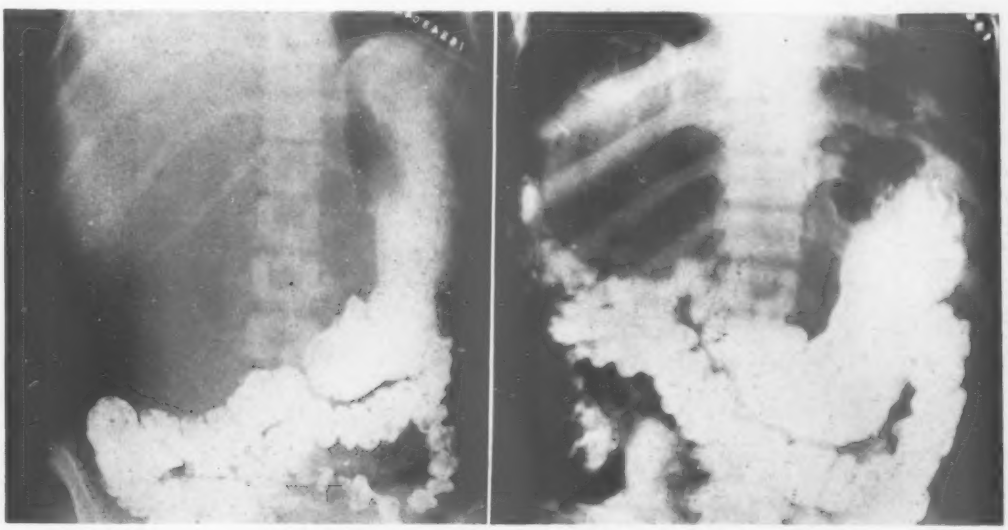
Corresponding to the hepatomegalia the adjoining organs, like the stomach, duodenum and the hepatic angle of the colon, all of which can be shown easily by the roentgenogram, are seen to be displaced. Frequently the cysts are situated in the inferior border of the liver producing displacement in the adjoining organs in the shape of a crescent (Fig. 7 and 8). These can be so marked that sometimes they simulate defects, especially of the lesser curvature of the stomach (Fig. 9). These displacements give valuable information as to the location of the tumor. But we have also seen cysts, containing as much as 2 liters of liquid, which produced no real enlargement of the liver and no division of the diaphragm and so no displacement of the adjoining organs (Fig. 10).

Sometimes liver cysts become infected without previous or subsequent perforation, forming pneumohydrocyst (Fig. 11, which shows a calcified double cyst, near the right diaphragm). This case healed after biological treatment, with diminution of the calcified region. Figure 12 shows a large pneumohydrocavity after operation.

Perforation of the liver cyst is not a rare occurrence and is nearly always accompanied by infection and a corresponding rise in temperature. But only in a case of an extensive perforation as, for example, into the digestive tract (Fig. 19), or into the bronchi (Fig. 18), is a pneumohydrocyst present.

The most frequent incidence of perforation is through the diaphragm and into the

Fig. 6. On the inner side of the right diaphragm a round crescentic shadow caused by a hydatid cyst of the liver.



Figs. 7 and 8. Crescentic shape of the hepatic angle of the colon due to displacement caused by a liver cyst on its lower surface.

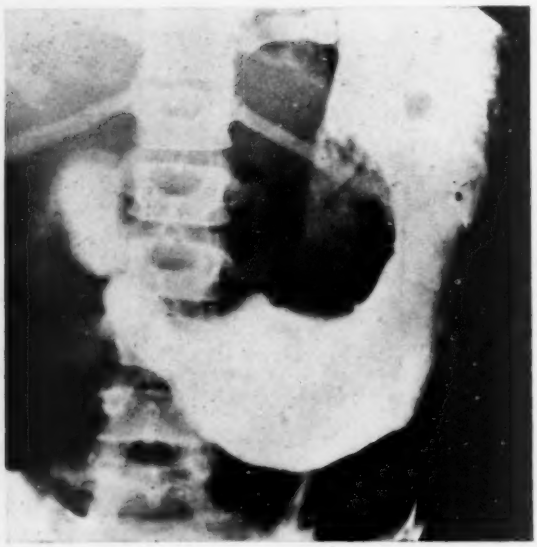


FIG. 9. Apparent filling defect of the stomach due to compression by a hydatid cyst in the left hepatic lobe.

FIG. 11. Pneumohydrocyst of the liver without demonstrable rupture. Calcified membrane (arrow). (Archives of Prof. B. N. Calcagno.)

bronchi. As a preclinical symptom one often sees impaired movement of the right hemidiaphragm and a slight accumulation of fluid in the right costodiaphragmatic sinus and an enlargement of the liver (Fig. 13).

The basal pneumonia that extends up to the hilum appears as lines (Fig. 14) or as a dense shadow (Fig. 15). If the cyst is also visible, there is no doubt as to the exactness of the diagnosis (Fig. 14 and 16). Occasionally the basal pneumonia is so dense in the frontal view that it hides the diaphragmatic deformations, caused by the cysts (Fig. 15) and the suspicious rounded shadow is only visible in the lateral view

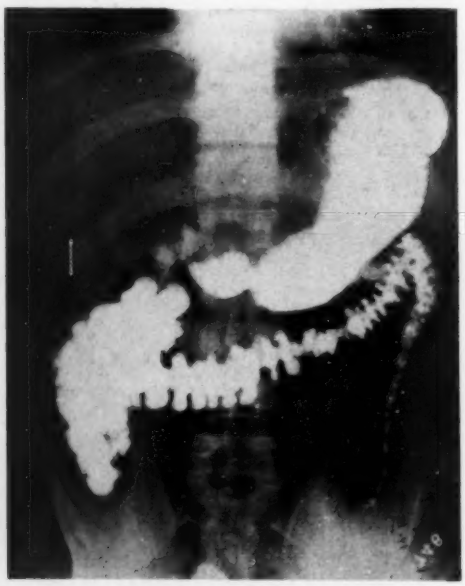


FIG. 10. Hydatid cyst of the liver, containing 1.5 liters, without apparent enlargement of the liver.

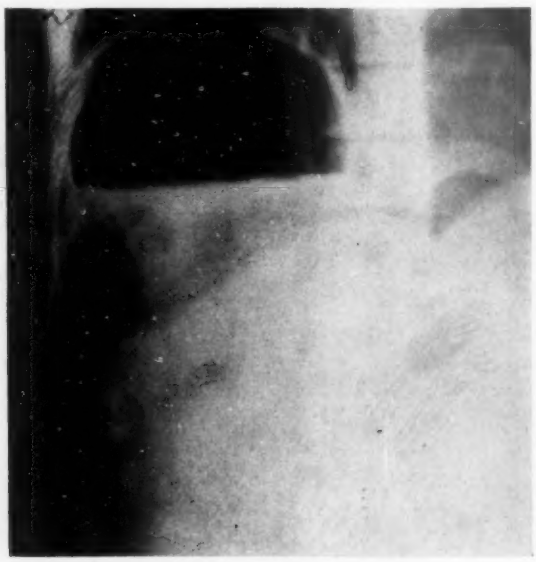


FIG. 12. Hydropneumatic cavity, three months after the removal of a liver cyst.

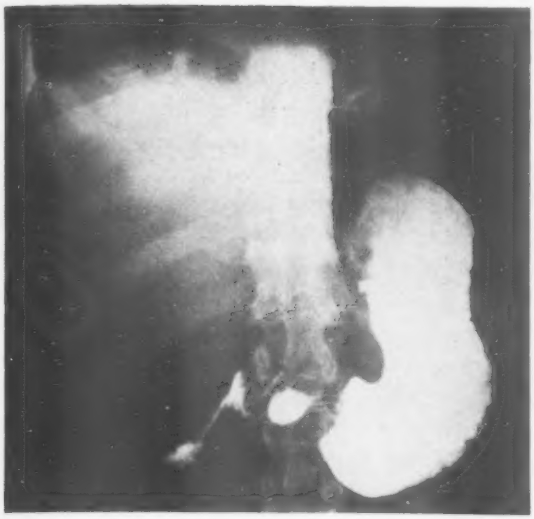


Fig. 13. Initial peridiaphragmatic perforation of a liver cyst. Large liver, some fluid in the right costodiaphragmatic sinus. Displacement of the stomach.

(Fig. 16). In these cases doubt arises as to whether it is a case of a perforated cyst of the base of the lung or the liver. Pneumothorax makes differentiation possible (Fig. 17), but this method is rarely employed, due to the great danger of pleural infection.

An ample opening of the cyst into a bronchus develops pneumohydrocysts in the liver (Fig. 18) with a membrane floating on the surface of the fluid.

Fig. 14. Calcified liver cyst perforated into the bronchi. (Archives of Prof. B. N. Calcagno.)

Fig. 15. Hydatid cyst of the liver perforated into the bronchi. Reactive basal pneumonia.

Perforation of the cysts into the bile ducts cannot be seen on roentgen examination.

Of course one can find occasionally a calcified cyst and nearly always displacements of the adjoining organs (we could never ob-

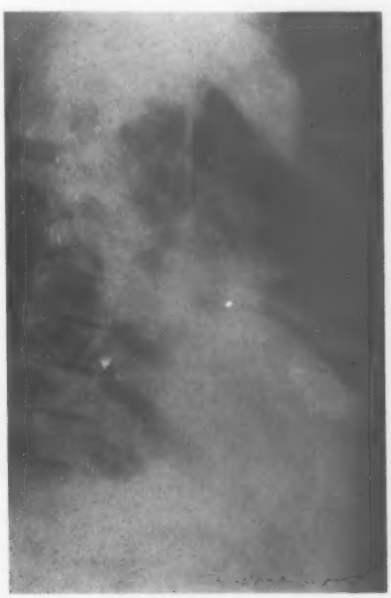


Fig. 16. Lateral view of the same case. Hydatid cyst visible.

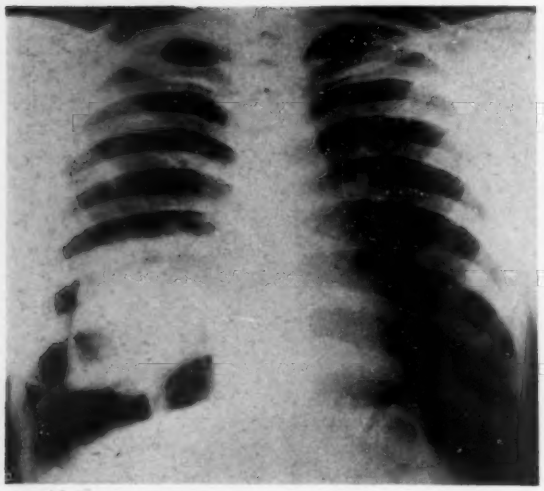


FIG. 17. Perforated lung hydatid cyst with pneumothorax, that proves its intrathoracic localization.

tain a positive cholecystogram in these cases). All this can help in arriving at a diagnosis, but only the presence of echinococcus hooks in the duodenal liquid is conclusive evidence.

Direct perforation into the digestive tract is rare. Figure 19 shows the dramatic picture of a perforation into the duodenum. The enormous pneumohydrocyst is clearly

FIG. 18. Pneumohydrocyst of the liver with floating membrane after perforation into the bronchi. (Archives of Prof. B. N. Calcagno.)

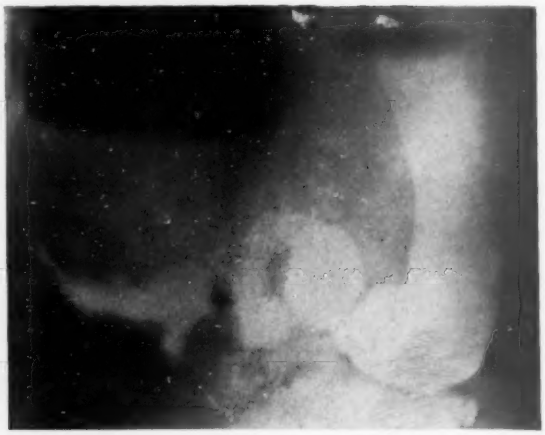


FIG. 19. Pneumohydrocyst of the liver after perforation into the duodenum. Floating membrane. Barium at the bottom of the cyst.

visible and also the membrane, floating on the surface of the liquid, in the form of an undulated line at the surface level known as the camalotes sign, which signifies a small floating island of tropical plants. The barium flows from the duodenum into the cystic cavity and settles down in the bottom of the cyst.

We saw another case of perforation into the hepatic angle of the colon with the same roentgen signs, the only difference being that the barium was carried by the enema through the intestine into the cavity.

We have seen cysts emptying through a fistula of the abdominal wall (transcutaneous). Filling with lipiodol showed a large

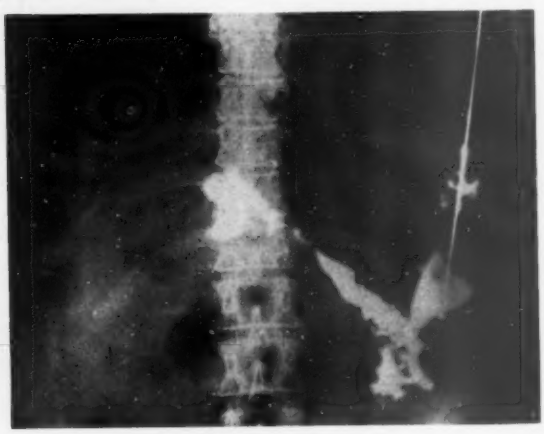


FIG. 20. Opaque filling of a fistula originated by a transcutaneous perforation of a liver cyst.

cavity and only operation revealed its hepatic origin. (Fig. 20).

ECHINOCOCCUS CYSTS OF THE ABDOMEN

In the opinion of many authors, multiple abdominal echinococcus cysts are usually the consequence of a rupture of a liver cyst into the abdominal cavity with the corresponding hydatid infection of the peritoneum. Usually they are accompanied by few clinical symptoms, which are easily missed. Years later the patient appears with a distended abdomen and symptoms of compression of the abdominal organs, the general state being unsatisfactory, sometimes with fever caused by suppuration of the cyst. Palpation of the abdomen gives the impression of an overfilled potato sack. Frequently the roentgenogram shows rounded shadows of the same density as the kidney (Fig. 21). More impressive are the displacements of the gastrointestinal tract, when filled by barium.

When the bladder, after injection with an opaque fluid, is seen to be displaced forward, metastatic cysts of the pouch of Douglas must be suspected (Fig. 22). Calcified abdominal cysts are rare. Pneumoperitoneum is not often employed for diagnosing cysts owing to the ensuing danger of tapping and its consequences.

Fig. 21. Abdominal hydatid cyst in the right lower abdominal region with soft shadow and dislocation of the kidney.

Fig. 22. Abdominal hydatid cyst in the pouch of Douglas with displacement of the opaque filled bladder. (Archives of Prof. B. N. Calcagno.)

ECHINOCOCCUS CYSTS OF THE SPLEEN

Those cysts of the spleen not calcified only give symptoms of displacement of the adjoining organs, due to the enlargement of the spleen (Fig. 23) Very great displacements can lead to doubt as to whether their origin is splenic or renal. Although the spleen usually displaces the splenic angle of the colon backwards, while the kidney displaces it forwards, sometimes not even a lateral view helps in making a differential diagnosis. The diagnosis is usually arrived at by means of pyelography, although the renal pelvis can be displaced and deformed by a large spleen, being indistinguishable roentgenologically from a closed cyst of the kidney.

ECHINOCOCCUS CYSTS OF THE KIDNEY

This is a more frequent occurrence and produces very illustrative findings. The simple roentgenogram shows great enlargement of the kidney, at other times only the

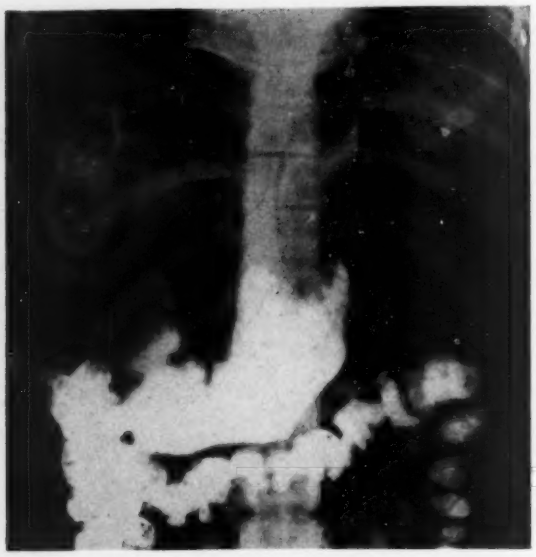


FIG. 23. Splenic cyst with displacement of the adjoining organs.

superior pole is enlarged. Occasionally calcifications can be seen (Fig. 24). The adjoining organs are always displaced. The pyelogram shows great deformity of the pelvis and the calices (Fig. 24). The picture is more clear cut if the cyst opens into a calix and through this medium into the urinary tract. In these cases the cavity fills with the opaque fluid (Fig. 25). Figure 26 shows a rare picture, where daughter cysts can be seen in the pelvis and another, deformed one, at the origin of the ureter and a third one in the bladder.

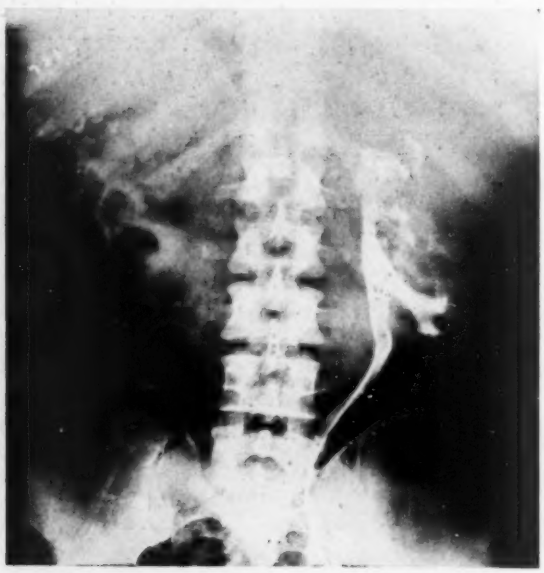


FIG. 24. Closed calcified hydatid cyst of the kidney with extensive deformation of the renal pelvis and of the calices.

ECHINOCOCCUS CYSTS OF THE BONES

These are very rare and we have seen only 4 cases, but Professor B. N. Calcagno has shown us 30 cases. At the beginning, when the involved bone is unchanged,

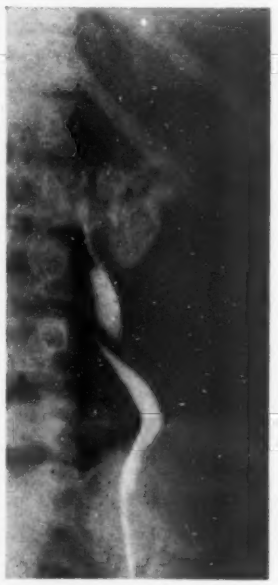


FIG. 25. Hydatid cyst of the kidney perforated into the renal pelvis.

either by infection or by operation, the roentgen appearance resembles surprisingly a giant cell tumor. The corresponding bone segment seems blown up and riddled with cavities (Fig. 27). The cortex is well preserved, although no reparative reaction of any kind is seen. At the same time in one case there was a large abscess in the axilla. We have never seen both appearances in giant cell tumor. Aspiration showed the remains of membranes.

If the cyst grows for a time, it invades the adjacent bones and soft parts with no respect for the anatomical limits. Extensive cyst defects, involving the adjoining bones and invading the cortex are frequent

Fig. 26. Calcified perforated hydatid cyst into the upper kidney pole with only slightly deformed pelvis. Daughter cysts visible in the pelvis, ureter and bladder. (Archives of Prof. B. N. Calcagno.)

in the pelvis and femur. Pathological fractures and small formations of sequestra in the adjacent soft tissue are frequently seen (Fig. 28). Lung cysts sometimes coexist.

Fig. 27. Hydatid cysts of the scapula. Blown bone, riddled by cystic defects. No reparation. Small sequestrum in the upper border of the scapula. (Archives of Prof. B. N. Calcagno.)

Fig. 28. Widespread hydatid cysts of the femur with pathological fracture and spotted shadows of the soft parts.

After surgical intervention the formation of fistulae and secondary osteomyelitis is frequent. A tendency to bone condensation and the disappearance of the cysts either totally or partially gives a misleading roentgen picture (Fig. 29). Otherwise, one sees extensive operative bone defect, not rarely combined with bone fracture and progres-

Fig. 29. Hydatid cysts of the pelvis, years after operation with numerous fistulas and membrane evacuation. Around the articulation osteomyelitic condensation of the bone. Cystic formation in the blown pubis and ischium. (Archives of Prof. B. N. Calcagno.)

FIG. 30. Hydatid cysts of the pelvis and femur, years after the operation. No osteomyelitis. Defects caused by operation and fractures. Cystic defects at the edges.

sion of the cyst towards the periphery (Fig. 30).

Especially difficult is the roentgenological diagnosis of the relatively frequent echinococcosis of the spine. Though the roentgen signs are insignificant at the beginning, it clinically produces the most alarming symptoms, originated by an extensive and plane infiltration of the meninges by cysts. Spinal blocks occur early (Fig. 31) and this is clearly visible after the myelography. Frequently one sees in the initial stage a partial destruction of the transverse processes, far below the block (Fig. 31) and a small, clear, bubble-like area of the lower adjacent vertebral body

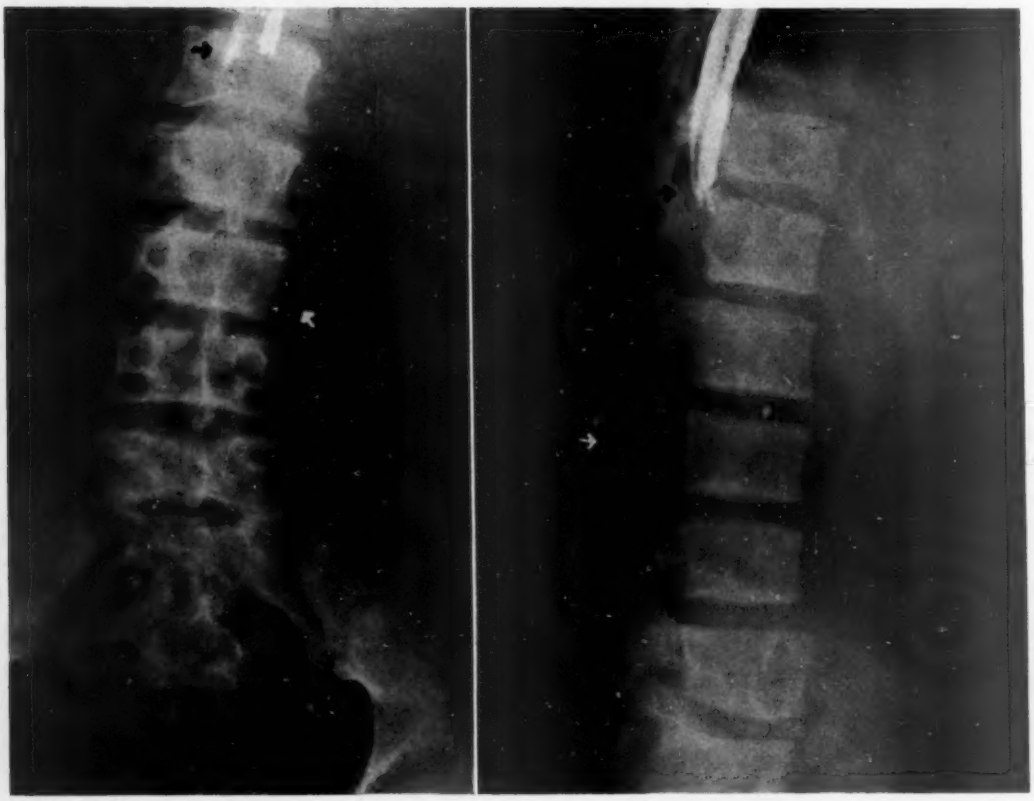


FIG. 31 FIG. 32

FIGS. 31 and 32. Initial hydatid cysts of the spine, destruction of the left transverse process of L_3 (Fig. 31) and bubble-like area of the vertebral body of L_3 (Fig. 32). Lipiodol block at the height of L_1. (Archives of Prof. B. N. Calcagno.)

(Fig. 32). Ossifluent abscesses are frequent and can be seen early in the dorsal spine (Fig. 33). The intervertebral discs escape involvement for a long time. If the disease progresses, destruction increases, the bubble-like character of the bone lesion disappears, the destruction progresses and attacks many vertebrae, but shows no tendency to destroy the disc (Fig. 32). With formation of spontaneous or operative fistulas, the roentgen picture becomes blurred by the accompanying osteomyelitis (Fig. 34).

HYDATID CYSTS OF THE LUNG

Twenty-two per cent of our cases have been found in the lung. The closed ones are roentgenologically different from the open ones. The closed cyst, which usually does not contain daughter cysts, appears roentgenologically as a round homogeneous shadow in the lung parenchyma (Fig. 35). This cyst, being of an expansive nature, makes the intercostal spaces bulge. The ribs are hidden by the opaque cyst shadow. The bone is not eroded, as it is in the extrapulmonary cysts of the pleura (Fig. 33).

FIG. 34. Repeatedly operated hydatid cysts of the spine with fistulae. The picture is blurred by the concomitant osteomyelitis. The intervertebral discs are destroyed. (Archives of Prof. B. N. Calcagno.)

FIG. 33. Extensive destruction of the right side of the 5th, 6th, 7th and 8th thoracic vertebrae and the corresponding ribs. Ossifluent abscess. Artificial shadow at the height of Th_4. Finding at operation: Extrapulmonary hydatid cyst of pleura with lesion of the bones caused by compression. Biopsy of the bone does not show hydatid invasion.

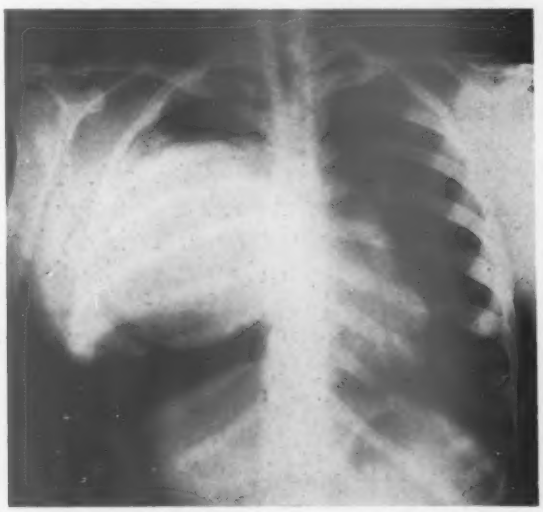


FIG. 35. Round sharply defined shadow of hydatid cyst in the right lung.

FIG. 36. The same case in lateral view shows polycyclic formation.

We have never seen calcified lung cysts and know of only one case in the literature. The movements of the diaphragm are seldom interfered with. As the cyst grows, it often loses its roundness and becomes polycyclic, being more often visible in lateral views (Fig. 36). The sharp limits disappear, due to a thickening of the pericystic membrane. These fibrous lines radiate into the surrounding lung parenchyma and also obscure the cystic image (Fig. 37). These findings make a differentiation from other round lung tumors diffcult. It is obvious that other roentgen signs must be found for a differential diagnosis. The first and simplest way is to look for other possibly calcified cysts, for they are quite frequent in the liver. If these are not found and other clinical symptoms do not give further help, one has recourse to bronchography.

There is no doubt that the *Echinococcus* only causes displacement of the bronchi that surround the cyst in a rather typical manner like a hand grasping the tumor in its fingers. Only the smallest bronchi are not permeable, owing to the compression, and they end in a point. It is a fact that the same deformity of the bronchi is caused by all benign tumors. But these latter being extremely rare, the presence of this sign in an endemic region arouses suspicion of hydatid cyst. But at times true bronchial block image is found in bronchograms of cysts. We have seldom used bronchography.

Other positive signs are the surprising movements and deformities of the soft and liquid containing cysts, which accompany changes in the position and in deep breathing. Unfortunately this sign is not of much help, because this form of deformity is also seen in other tumors. It is not real change in the shape of the tumor, but an altering of the roentgen shadow, due to change in position.

The existence of large round shadows in both lungs makes the diagnosis of hydatid cyst almost certain (Fig. 38).

Small multiple cysts, in both lungs, cannot be differentiated roentgenologically from metastatic neoplastic processes (Fig. 39). Although multiple cysts are really metastatic processes, we saw the appearance in 2 cases three months after the removal of liver cysts, the lungs having been free of cysts before operation. If a cyst bursts,

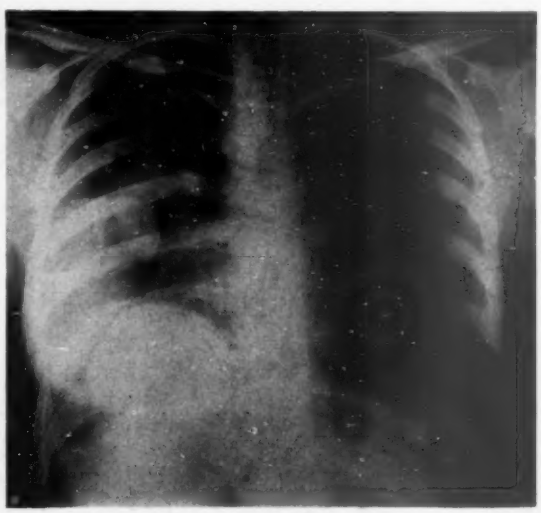


FIG. 37. Multiple hydatid cysts in the middle and lower part of the left lung. The shadow, adjoining the hilum shows network of lines.

Fig. 38. Large bilateral lung cysts with irregular border.

and the level of the liquid is visible in one of the multiple round shadows, then the roentgen diagnosis is assured (Fig. 40), but in these cases, the clinical and the laboratory findings have decided the question beforehand.

The rupture of a lung cyst is sometimes foretold by the appearance of a pericystic emphysema. Above the cystic shadow and sometimes behind it there appears a transparent air shadow, in the shape of a crescent, which corresponds to an accumulation of gas between the pericystic and the cystic walls (Fig. 41). Sometimes the emphysema is so small that it can be seen only by tomography. Though Professor F. Dévé states that a peritumoral emphysema can be found also in non-cystic tumors, the sign

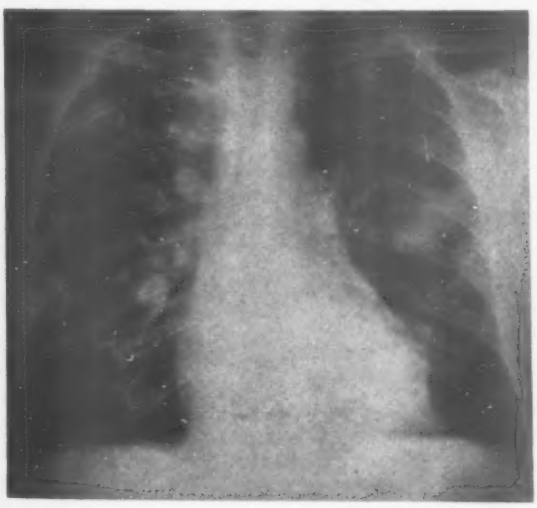


Fig. 39. Small spotted metastatic lung cysts.

Fig. 40. Small spotted metastatic lung cysts. On the left side a pneumohydrocyst.

Fig. 41. Pericystic emphysema. One sees a convex border not altered by changing position (no fluid). (Archives of Prof. B. N. Calcagno.)

FIG. 42. Dry membrane at the bottom of a pneumocyst. Right above large round hydatid cyst.

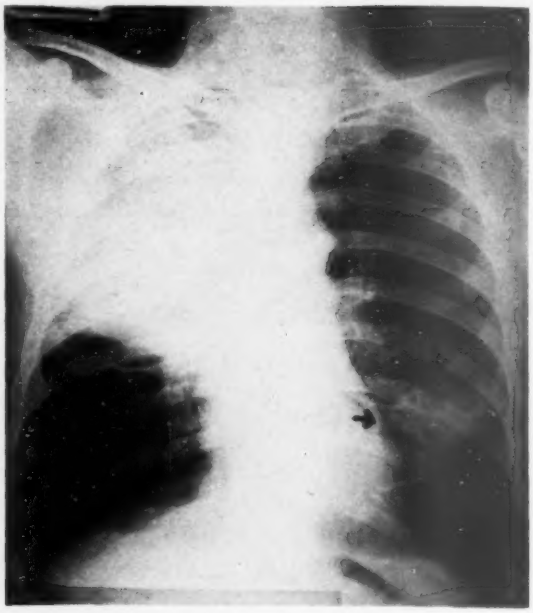


FIG. 43. Same case. The pneumocyst is resorbed and the membrane lies in a closed cavity (incarcerated membrane). The large cyst, right, above, has burst causing a pneumonic massive infiltration. (Archives of Prof. B. N. Calcagno.)

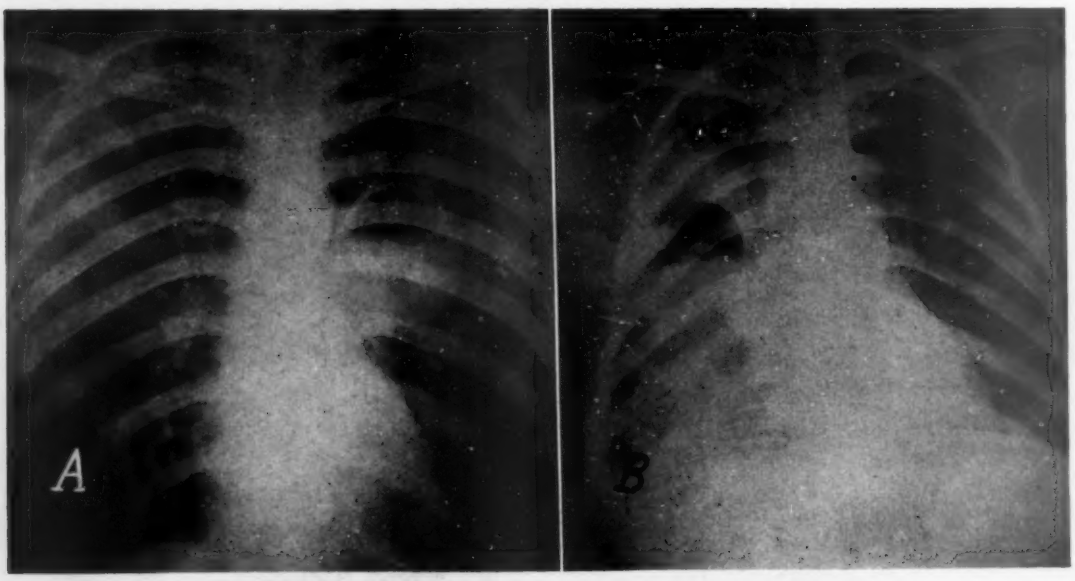


FIG. 44. *A*, floating membrane in a hydropneumocyst. *B*, sign of double arch. (Archives of Prof. B. N. Calcagno.)

is very useful for diagnosis of echinococcus cyst. It is not certain whether it originates through a communication between the bronchus and the pericystic cavity, or from the rupture of an adjoining emphysematous bulla. It could also be caused by the shrinking of the echinococcus cyst after its degeneration. This pericystic emphysema signifies the death of the parasite. Clinically this phase manifests itself by small hemoptyses.

The clinical evolution, as well as the roentgen signs, varies. Sometimes there is a progressive drying and reduction in size of the cyst. Roentgenologically the pericystic emphysema persists, the parasite diminishes in size and becomes transparent and its membrane folds up and falls to the bottom of the cavity (Fig. 42). This process is progressive until all the air of the cavity is resorbed. The pericystic membrane lies close to the cystic membrane (incarcerated membrane, (Fig. 43).

Sometimes this clinical and roentgenological picture remains at this stage for years. More frequently there is reactivation and suppuration with abscess formation.

Rarely the shrunken cyst bursts and pours out some fluid giving a surprising roentgen picture (Fig. 43). The superior

Fig. 45. Floating membrane in a pneumohydrocyst. Extensive accompanying pneumonia.

rounded border corresponds to the lung substance. Below there exists a transparent crescentic area, corresponding to the pericystic emphysema, bounded below by a fine line, which is the pericystic membrane. The cyst contains some air and liquid (hydropneumocyst with floating membrane). This is called the sign of the double arch.

In other cases the rupture of the cyst is accompanied from the beginning by marked and widespread inflammation and ate-

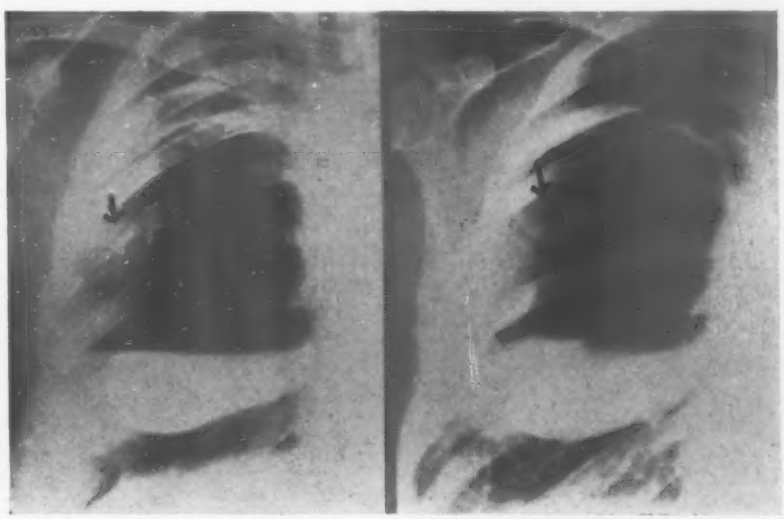


Fig. 46. Hydropneumocavity. Immediately (left) and years after operation (right).

lectasis of large areas of the lung. The round cyst shadow (Fig. 42, above) changes in a few days into a compact lobar shadow (Fig. 43, right above, being taken from the same patient, as the previous roentgenogram) which shows no cavity either in the tomogram or in a penetrating roentgenogram, because the cavity is full of liquid. In these cases bronchography sometimes is enlightening.

In other cases one sees in the infiltrated lung parenchyma a pneumocyst or a hydropneumocyst, in rare cases with camalotes (Fig. 45).

The further development of the described cavities is different. Some disappear without treatment, others with biological treatment and yet others need pneumothorax or surgical intervention. Figure 46 shows postoperative hydropneumocavity which is nearly unchanged after three years, although the resected rib had time to regenerate.

I would like to express my very grateful thanks and appreciation to Professor B. N. Calcagno and his very able assistant Dr. J. C. Casiraghi for their invaluable and most unselfish help, in furnishing me with some of their best material.

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IRRADIATION OF PITUITARY TUMORS*

RESULTS IN FIFTY CASES

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THE object of this paper is two-fold: (1) to present the general subject of the diagnosis and irradiation of pituitary tumors and (2) to report the results of a follow-up survey of 25 cases presented in 1941, with a review of an additional series of 30 cases.

Embryologically the pituitary body or gland is developed from two sources. The anterior or glandular portion is derived from an upgrowth of the pharyngeal mucosa known as Rathke's pouch or the craniopharyngeal duct, while the posterior portion develops from a downgrowth from the floor of the third ventricle and is of nervous origin. The craniopharyngeal duct ordinarily disappears but rests may remain in any part of its course and these may later give rise to cystic or solid craniopharyngiomas or Rathke's pouch cysts or tumors. These ordinarily occur in the suprasellar region but may also be found within the pituitary body and masquerade as tumors of the hypophysis itself. This must be kept in mind when dealing with cystic tumors. The pars intermedia is an epithelial structure which covers the posterior portion and lines the gap which separates the anterior from the posterior "lobe."

The anterior lobe is composed of chromophilic and chromophobic cells formed in columns and surrounded by large blood spaces. The chromophilic cells can be divided into eosinophilic and basophilic types; the former are more abundant in the center of the gland while the basophilic cells are more numerous at the periphery.

Physiologically, the anterior lobe cells have mainly to do with growth and sexual development while the posterior lobe elements are concerned with carbohydrate metabolism and consequently development of fat.

In this study we are interested in the tumors or hyperplasias which develop in the anterior lobe and which because of their size, or abnormal hormone secretion, or both, cause a variety of symptoms.

The diagnosis of pituitary tumor is usually made by the neurologist or ophthalmologist in consultation with the radiologist, although, because of symptoms referable to the thyroid, the patient may first consult an internist or possibly an orthopedist, if weakness of the back is an early symptom, as it may be when growth is rapid.

I shall consider first eosinophilic or acidophilic tumors. These lesions are suspected mainly because of their hormonal activity which is usually of the growth type. If the tumor occurs before the closure of the epiphyseal lines, the patient develops gigantism. With the development of gigantism, complaints of a weak and somewhat painful back may also be present. If the tumor develops after normal growth has ceased, acromegaly is the result—large hands and feet, prominent jaw, enlarged head and sinuses. It must also be remembered that there may be an increase in the thyrotropic hormone with a resultant increase in the basal metabolic rate and diffuse enlargement of the thyroid gland. We have seen 2 such cases, in 1 of whom the basal metabolic rate became normal after irradiation. Patients with acidophilic pituitary tumors may also complain of headaches and study of the visual fields frequently shows bitemporal cuts, which indicates pressure on the optic chiasm. Occasionally no changes whatsoever can be found in the fields. In our ex-

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perience, approximately 60 per cent of the cases of acidophilic tumor of the pituitary showed roentgenographic evidence of enlargement or erosion of the sella turcica. Amenorrhea and loss of libido are mentioned as of frequent occurrence but in our experience these have not been of outstanding importance. Increased sexual activity in both sexes is said to be present early with this type of adenoma. Headache, however, may be the presenting symptom. These tumors do not ordinarily become as large as chromophobic adenomas because their symptomatology is more arresting.

The chromophobic cells have no definite known function and a tumor composed of this type of cell produces signs and symtoms due to its size alone—i.e. pressure symptoms. These may be (1) headache, because of pressure on the sella and diaphragma sellae. Following a considerable period of increasing severity, there may be relatively sudden relief from headache due probably to rupture of the diaphragm or fracture of the dorsum sellae with release of pressure. This loss of headache must not be thought of as improvement in the patient's basic condition, however. (2) Increase in the size of the tumor causes increased pressure on the acidophilic group of cells with resultant atrophy and the development of hypopituitarism. This results in weakness, fatigability, decrease in libido in the male and amenorrhea and sterility in the female. These changes may be so insidious, however, that the tumor may go unrecognized until it has reached sufficient size to press upon the optic chiasm. When this occurs, changes are noted first in the superior temporal quadrants of the visual fields. The slowness of development of this symptom accounts, no doubt, for the fact that almost complete loss of the temporal fields may occur before the patient is aware that he is losing his vision. If there is extension of the tumor laterally and posteriorly, there may be involvement of the third, fourth and sixth nerves with resultant ophthalmoplegia. In our experience, increased intracranial pressure beyond that confined within the sella is practically unknown. This is said by some to occur commonly but in only 2 of our cases was there any suspicion of such an occurrence. Types I and II may also occur together and form a mixed group of cases.

The third general type of pituitary tumor is the basophilic adenoma which causes the well known but infrequently seen cases of Cushing's basophilism. These tumors are small, cause no enlargement of the sella and ordinarily no headache. The cardinal symptoms are change of facies, hirsuitism, hypertension, abdominal striae, painful adiposity of the face, neck and trunk and sexual dystrophy. It must be remembered that a similar syndrome can arise because of certain adrenal tumors.

TREATMENT

The original treatment for tumors of the pituitary gland was surgical and occasionally this method is still used primarily. More and more, however, it has become recognized that irradiation should be used first, and only if this fails should the patient be operated on. Gramegra, in 1909, is usually credited with having been the first to use irradiation for the treatment of a pituitary tumor. The first permanent result, however, was probably in a case treated by Béclère. His patient, treated in 1909, was well twenty-two years later.

Our method of treatment is radically different from most other present day techniques only in that we do not give repeated courses but try to deliver to the tumor in one course all the radiation which is necessary to cause regression, just as we do with malignant tumors. This consists of treating through four fields directed toward the sella turcica—two temporal, one frontal and one vertical. We use 200 kv., with a quality of 1.95 mm. Cu half-value layer, 50 cm. distance and a 5 cm. cone. One hundred roentgens are given to one field the first day in order to reduce to a minimum the chances of causing swelling with increased intracranial pressure and

headache. If no reaction ensues, two fields are given 100 roentgens each the second day and from then on 200 roentgens are given to each of two fields per day. This is carried up to a total of 2,000 roentgens per field (air dose). With the ordinary sized calvarium, this delivers approximately 2,400 roentgens into the pituitary fossa. There is, of course, temporary epilation over the treated hair-bearing area but we have never seen the epilation become permanent. Until about five years ago, we treated these cases over an additional occipital field and carried the total air dose to 9,000 roentgens. We also sometimes used fields larger than 5 cm.—usually 6 by 8 cm. This gave a considerably larger tumor dose which was routinely between 3,000 and 3,600 roentgens.

In the previous report, we divided our results into "excellent," "good" and "poor" depending upon whether (1) there was an increase in visual fields, loss of headache and general improvement in the patient's over-all condition, (2) arrest of the process with loss of headaches and (3) no demonstrable good effects of the treatment. The results of the treatment of 25 cases at that time were reported as excellent, 56 per cent; good, 20 per cent; poor, 24 per cent. All but one of the living cases have been followed. One case was proved not to be a tumor of the pituitary so the series is reduced to 24 cases of which 14 (58.3 per cent) had excellent, 5 (20.8 per cent) good, and 5 (20.8 per cent) poor results, or excellent and good 79.1 per cent. Of the 5 failures, 1 died fifty-two months after having shown improvement for nineteen months; 1 died one month following treatment; 1 died with cerebral symptoms attributed by us to a combination of hypertension and irradiation; and 2 were unimproved and at operation cystic tumors were found. These 2 cases have done well postoperatively.

The second series is not quite so easy to evaluate because 2 of the patients were too sick to tolerate treatment and are excluded from the series studied statistically. Two others were admitted from institutions for the insane and were obviously psychotic. They were also practically blind. Although they are both living, the mental deterioration has progressed and blindness was not affected. They also have been omitted from the series. That leaves 26 cases and of these 15 (57.7 per cent) had excellent, 3 (11.5 per cent) good, and 7 (26.9 per cent) poor results; or excellent and good 69.2 per cent, poor 30.7 per cent.

For the entire series of 50 cases, 29 (58 per cent) had excellent results, 6 (12 per cent) had good, and 15 (30 per cent) had poor results; or 70 per cent excellent and good results.

Of the total of 50 cases being reported on, there are 11 acidophilic, 1 basophilic, 37 chromophobic and 1 mixed acidophilic and chromophobic. Seventy-two per cent of the acidophilic group did well while 70 per cent of the chromophobic tumors had excellent or good results. Our 1 case of basophilic tumor did poorly. The ages ranged from eleven to seventy years. Twenty-six of the total series were women and 28 were men and boys.

COMMENT

We think that all types of pituitary tumor—acidophilic, basophilic, and chromophobic—should receive primary irradiation. It has been said many times that only acidophilic adenoma is sensitive to irradiation. With this we do not agree. The chromophobic does equally well. There are at least three suspected conditions, however, which we think should make one defer radiation therapy: (1) suspicion of a cystic tumor, (2) symptoms of hemorrhage into the tumor and (3) increased intracranial pressure. It is almost universally agreed that it is futile to irradiate a cystic tumor. The tumor may be cystic because of a developmental anomaly arising from remnants of the craniopharyngeal duct, from degeneration of the tumor, or from an old hemorrhage. It is almost impossible, however, to be at all sure that one is dealing with a cystic tumor before irradiation or surgical interference. It is of the utmost im-

portance that patients having any constriction of the visual fields should have these tested frequently and if there is continued decrease in the fields two months following the cessation of therapy, operation should be advised at once. It must be remembered, however, that there is not uncommonly an early further constriction of the fields during irradiation and this should not deter one from giving the full course of treatment.

It is easier to suspect recent hemorrhage into a tumor because there is a history of an acute episode, following which there is sudden onset of visual disturbance. We have seen one such case during the past year. Only once have we suspected a cystic tumor in time to refuse to give irradiation. I must stress again the necessity of careful repeated visual field determination up to at least two months following cessation of the irradiation. Increased intracranial pressure is of such infrequent occurrence in our experience that it is not much of a factor. Should it occur, however, I think that the primary approach should probably be surgical with postoperative irradiation.

The diagnosis of adenoma of the pituitary is not always as simple as it seems. In the cases of acidophilic tumor one must rely on the signs of growth disturbance, secondary hypopituitarism or perhaps secondary changes in the thyroid. Enlargement of the sella turcica and visual field changes are not necessary. When diagnosing chromophobic adenoma, however, we have three times encountered difficulty. The first case had an enlarged sella, visual field changes and headaches and was diagnosed as a case of pituitary tumor. Following irradiation, he did well for five years. He then had recurrent difficulty and operation revealed an epidermoid carcinoma of the pineal. This is the case that was removed from the 1941 series. The second was a fat boy with enlargement of the sella and field constrictions. For about a year he showed improvement following treatment. He then became worse and died promptly. At autopsy, his osseous system was found riddled with Ewing's tumor. The third case was a man with a large sella and all signs of pituitary tumor of the chromophobic type. Because of bronchiectasis and blood streaked sputum, he had a bronchoscopy which revealed an epidermoid carcinoma of the bronchus. His intracranial lesion was undoubtedly metastatic.

Whereas it now seems wise to institute radiation treatment for all uncomplicated cases of pituitary tumor—and by uncomplicated I mean without hemorrhage or with no suspicion of cyst formation—it appears logical to lean heavily on the neurosurgeon when these complications occur or are suspected. Thus all cases not showing adequate response in two months should be operated on, and cases operated on primarily should have postoperative irradiation because ordinarily not all of the tumor can be removed without sacrificing at least one of the optic nerves. Four of the irradiation failures that were operated on have remained well for from 54 to 103 months. There were 3 postoperative deaths.

COMPLICATIONS

Camp has reported several cases of radiation necrosis of the skull following treatment for pituitary tumor. So far we have seen only one case of radiation necrosis of the skull and that was in a case we had treated intensively for a brain tumor—not pituitary. Our experience with more than 50 cases indicates that the danger of this complication is small and can be essentially disregarded, if the technique outlined above is used.

In irradiating the brain with heavy doses we must be careful not to exceed the usually accepted maximum tissue dose of from 4,500 to 5,000 roentgens. We have never seen any indication of damage to the brain in the treatment of such lesions, even at autopsy, as we have following intensive treatment for glioma of the brain. Perhaps twice, we have seen symptoms suggesting increased intracranial pressure following

TABLE I

Case	Name	Age	Sex	Signs and Symptoms	Tumor Type	Treatment	Progress	Months Followed Result
1	C. A. First series	69	M	Diplopia; failing vision for 4 mo.; bitemporal hemianopsia; enlarged sella; vos 6/12; vod 6/15 plus 2	Chromophobe	Oct. 1938. Tumor dose 2,546 r in 27 days	Visual fields enlarged 2 mo. after treatment. Unchanged, thereafter. Died 12-18-39 of proved coronary occlusion	14 mo. Good
2	L. A. First series	43	M	Failing vision for 1 yr. with blindness os 6 mo.; occipital headaches; temporal hemianopsia od; enlarged sella	Chromophobe	Feb. 1934, 1,600 r in 15 days. Dec. 1934, 2,457 r in 23 days. April, 1935, 1,931 r in 19 days. Total: 5,988 r in 14 mo.	Vision improved after 9 mo. Gradually improved. Vision in blind eye returned to ½ field	144 mo. Excellent
3	N. A. Second series	31	F	Increase in size of hands and feet for 18 mo. Decrease in lateral vision	Chromophobe? Mixed?	Nov. 1941, 8,000 r in 28 days. Tumor dose 2,643 r	Increase in fields to normal	54 mo. Excellent
4	W. A. First series	62	M	Headaches for 8 mo.; diplopia for 3 mo.; ptosis for 1 mo.; ophthalmoplegia; destruction of sella and of anterior portion of foramen magnum	Chromophobe	Aug. to Oct. 1939, 3,831 r in 47 days	Headache improved. No ptosis of right upper lid. Felt generally better	20 mo. Good
5	A. B. Second series	34	M	Acromegaly	Acidophilic	June 1940, 8,600 r in 26 days. Tumor dose 3,500 r	No progression of symptoms. Good vision	72 mo. Excellent
6	W. B. Second series	35	M	Visual loss	Chromophobe	May 1941, 9,000 r in 28 days. Tumor dose 3,217 r	Gradual improvement	61 mo. Excellent
7	W. B. First series	44	M	Enlarging hands and feet for 4–5 yr.; acromegalic features; sella enlarged; B.M.R. plus 40%; visual fields normal	Acidophilic	Nov. 1934, 1,200 r (air) to each of 5 portals in 22 days.	In 3 mo. hands and feet felt smaller and patient felt better; 57 mo. later B.M.R. plus 14%; facial expression unchanged	140 mo. Excellent
8	C.E.C. First series	30	M	Failing vision to shadow perception os for 18 yr.; 42 lb. increase in weight; sella enlarged; vos blind; vod temporal field loss	Chromophobe	Partial surgical removal 2 yr. before irradiation. May 1931–May 1932, 4,000 r (air) with 200 kv. 0.5 mm. Cu., 1.0 mm. Al, and 5,400 r (air), 130 kv. 0.25 mm. Cu, 1.0 mm. Al	Improved following operation but blind 2 yr. after irradiation; field larger; 115 mo. vision showed no improvement.	160 mo. Good
9	W.E.D. Second series	22	M	Failing vision for 6 yr.; bitemporal cuts; od almost blind; enlarged sella	Chromophobe	May 1942, 8,000 r in 23 days. Tumor dose 3,217 r	Died 1 mo. after irradiation. Operation showed large tumor arising from sella. Increased intracranial pressure; 280 mm. water; contents removed; no pathology	1 mo. Poor
10	M. D. First series	70	F	Blurred vision for 3 yr. occipital headaches; enlarged sella; bitemporal hemianopsia	Chromophobe	May 1939, 1,516 r in 13 days. Nov. 1939, 1,766 r in 17 days. Total: 3,284 r in 6 mo.	Divided dosage because of age. 3 mo. after second course visual acuity improved. Fields unchanged; 21 mo. after first course able to write but vision not improved. Later follow-up, gradually failing vision	84 mo. Good
11	L. E. Second series	58	F	Enlarged sella; bitemporal cuts	Chromophobe	Feb. 1941, 9,000 r in 28 days. Tumor dose 3,672 r	Questionable improvement. Died with pituitary adenoma in June 1946. At postmortem tumor showed no evidence of having been irradiated	65 mo. Poor

Table I—(*continued*)

No.	Name	Age	Sex	Signs and Symptoms	Tumor Type	Treatment	Progress	Months Followed Result
12	B. F. Second series	49	F	Bilateral optic atrophy; od blind; os complete temporal cuts	Chromophobe	Sept. 1940, 9,000 r 27 days. Tumor dose 3,619 r	Some improvement in sight	68 mo. Excellent
13	G. F. Second series	68	M	Enlarged sella; bitemporal cuts; od almost blind	Chromophobe	June, 1943, 8,000 r in 24 days. Tumor dose 2,606 r	Increase in fields; os, od practically blind	35 mo. Good
14	V.M.E. Second series	35	M	Bitemporal cuts for 23 yr.; enlarged sella	Chromophobe	Oct. 1941, 8,000 r in 24 days. Tumor dose 3,397 r	Loss of headaches. Good vision od; drives car	55 mo. Excellent
15	L. G. Second series	22	F	Amenorrhea for 2 yr.; acromegaly; loss of vision over 2–3 yr.; optic atrophy on right; enlarged sella	Acidophilic	Nov. 7—Dec. 7, 1940, 3,420 r in 27 days, tumor dose	Visual fields returned to practically normal on the right; left eye still blind	76 mo. Excellent
16	G. H. First series	46	M	Blind od 21 mo.; failing vision os 3 mo. mentally dull; B.M.R. minus 31%; sella enlarged	Chromophobe	Aug. 1934, 1618 r in 13 days. Nov. 1939, 1766 r in 17 days. Total: 3,284 r in 6 mo., tumor dose	Visual fields os smaller after first course. Visual fields os larger 6 mo. later. B.M.R. minus 24%. Improved for 19 mo. At 52 mo. died suddenly. Autopsy showed 2×4 cm. sellar tumor	52 mo. Poor
17	V. H. Second series	70	F	Headaches; loss of vision; enlarged and eroded sella	Chromophobe	April 1944, 2,540 r in 28 days, tumor dose	Could read and write in 2 mo.	2 mo. Excellent
18	R. H. First series	50	M	Failing vision os 12 mo. failing vision od 3 mo. bitemporal hemianopsia; enlarged sella	Chromophobe.	Oct. 1939, 2,990 r in 37 days, tumor dose	3 mo. after therapy vision improved; 15 mo. still further improvement. 54 mo. died of pneumonia	54 mo. Excellent
19	H. H. First series	62	F	Blurred vision and dizziness for 3 yr.; coarse hands and feet; visual fields contracted; heart failure	Acidophilic	Oct. 1932, 3,222 r in 23 days, tumor dose	Died 1 mo. after therapy	1 mo. Poor
20	E. J. First series	28	F	Weight increase of 130 lb. in 10 yr.; enlarged sella; no visual disturbance; frequent headaches	Chromophobe	March 1934, 1000 r in (air) to each temporal area. Sept. 1934, repeated above	Headaches relieved for 81 mo. after first course. No weight gain	144 mo. Excellent
21	T. J. Second series	30	F	Acromegaly; back pain; binasal field cuts; headaches	Acidophilic	June 1942, 8,000 r in 25 days. Tumor dose 2,480 r	Loss of headaches. Increased constriction of fields. Decrease in fields made operation imperative. Found hemorrhagic cyst. Practically all removed. Recurrence probably prevented	47 mo. Poor for roentgen irradiation. Good surgically
22	J. K. First series	68	M	Failing vision for 5 yr.; headaches; bitemporal hemianopsia; enlarged sella	Chromophobe	Sept. 1936, 3,148 r in 23 days. Further treatment elsewhere 1937–1938, amount unknown	42 mo. after treatment, no headaches; vision fair. Died of cerebral accident	42 mo. Good
23	L. K. First series	35	M	Failing vision and headaches for 18 mo.; complete temporal hemianopsia os; clinoids thin	Chromophobe	Oct. 1939, 3,043 r in 48 days	Visual acuity improved; fields unchanged; headaches improved. Good result in 23 mo.	81 mo. Excellent

TABLE I—(*continued*)

No.	Name	Age	Sex	Signs and Symptoms	Tumor Type	Treatment	Progress	Months Followed Result
24	M. L. Second series	21	F	Acromegaly and gigantism; loss of temporal cuts	Acidophilic	April 1941, 9,000 r in air in 27 days	Vision normal; generally good health	61 mo. Excellent
25	A. L. Second series	60	F	Acromegaly	Acidophilic cystic	May 1941, operated on—60 cc. of fluid aspirated with drainage of frontal lobe. 9,000 r in 27 days. Tumor dose 3,700 r	Operated on after irradiation. Died three days later. No autopsy	1 mo. Poor
26	E. L. Second series	30	M	Acromegaly; headaches; enlarged sella; no visual field changes	Acidophilic	Sept. 1944, 3,080 r in 23 days, tumor dose	Loss of headaches; general good health	11 mo. Good
27	B. L. Second series	19	F	Amenorrhea; hirsutism; hypertension	Basophilic	Aug. 1942, 2,157 r in 15 days, tumor dose	Seemingly improved for 1 week; sudden death with low blood pressure	1 wk. Poor
28	F. L. First series	48	F	Failing vision for 3 yr.; headaches; ptosis of right lid; enlarged sella; fields contracted	Chromophobe	Jan. 1939, 1,899 r in 21 days, tumor dose	Died 4 mo. after treatment; improvement in ptosis but developed mental confusion	4 mo. Poor
29	L. M. Second series	59	F	Acromegaly; trigeminal neuralgia; not much field cuts	Acidophilic	March, 1943, 8,000 r in 23 days. Tumor dose 2,485 r	Vision good	38 mo. Excellent
30	B. M. First series	36	F	Increasing weight for 13 yr.; headaches; enlarged sella; temporal field cut	Chromophobe	Dec. 1931, 819 r in 7 days, tumor dose	Good vision. Eyes weak unable to see to thread needle	108 mo. Excellent
31	M. M. Second series	41	M	Poor vision for 6 yr.; headaches; loss of vision greater in left eye than right	Chromophobe	April 1942, 8,000 r in 23 days. Tumor dose 3,355 r	Od same	94 mo. Good
32	O. M. Second series	36	F	Decreased visual fields; headaches; syphilis-meningovascular	Chromophobe	Sept. 1941, 8,000 r in 23 days	Increase in fields	51 mo. Excellent
33	J. P. First series	11	M	Increasing obesity for 3 yr.; headaches; sleepiness; right homonymous hemianopsia	Chromophobe	Sept. 1937, 2,866 r in 29 days, tumor dose	Rapid improvement in vision; loss of weight and gain in height; no headaches; with original class in school	108 mo. Excellent
34	J. H. P. First series	30	M	Headaches; failing vision; bitemporal hemianopsia; enlarged sella	Chromophobe	June 1936, 2,576 r in 25 days, tumor dose	Fields normal in 3 mo.	114 mo. Excellent
35	R. P. Second series	34	M	Acromegaly; bitemporal cuts; increase in size of hands, feet and head	Acidophilic	Aug. 1943, 8,000 r in 25 days. Tumor dose 2,620 r	Increased fields. Works normally	33 mo. Excellent
36	G. R. Second series	22	F	Amenorrhea; bitemporal hemianopsia	Chromophobe	Oct. 1943, 8,000 r in 23 days. Tumor dose 2,520 r	Slight improvement after nearly 2 yr.	32 mo. Excellent
37	C. R. First series	35	M	Headaches and blurred vision for 1 yr.; bitemporal hemianopsia; enlarged sella	Chromophobe	June 1935, 1,706 r in 16 days, tumor dose Jan. 1936, 2,152 r in 18 days, tumor dose	Gradual improvement in vision until 6 mo. post-irradiation, it was normal	132 mo. Excellent
38	C. R. First series	44	M	Bitemporal hemianopsia for 1 yr.; headaches	Chromophobe	Oct. 1937, 2,510 r in 25 days, tumor dose	Loss of headaches; vision slightly but definitely improved	104 mo. Excellent

TABLE I—(*continued*)

No.	Name	Age	Sex	Signs and Symptoms	Tumor Type	Treatment	Progress	Months Followed Result
49	P. R. Second series	15	M	Pituitary dwarf with sellar changes and field cuts; enlarged sella	Chromophobe	Oct. 1941, 8,000 r in 23 days. Tumor dose 2,640 r	Restoration of field cuts. Also received pituitary growth hormone	55 mo. Excellent
40	R. S. First series	39	M	Failing vision for 2 yr.; almost blind os for 1 yr.; headaches for 1 yr.; bitemporal hemianopsia; enlarged sella	Chromophobe	Jan. 1938, 2,047 r in 29 days, tumor dose May 1939, cystic tumor partially removed	Visual fields improved postoperatively	96 mo. Poor
41	A. S. First series	46	F	Blurred vision and headaches for 5 yr.; vos 6/6–1; temporal hemianopsia os; unable to obtain field od; enlarged sella	Chromophobe	April 1933, 3,120 r in 12 days, tumor dose	Loss of headaches and gradual improvement in vision. Glasses needed only for reading	156 mo. Excellent
42	L. S. Second series	48	M	Failing vision for 6 mo. Enlarged sella	Chromophobe	May 1943, 8,000 r in air in 24 days	Gradually became blind; paralysis agitans	37 mo. Poor
43	V. S. First series	58	F	Bitemporal hemianopsia; enlarged sella	Chromophobe	Nov. 1936, 2,129 r in 34 days, tumor dose	Slightly enlarged fields	116 mo. Excellent
44	J. T. First series	57	M	Failing vision; diplopia for 3 yr.; vod 6/24; vos counts fingers at 2 ft.; enlarged sella	Chromophobe	Jan. 1933, 3,820 r in 34 days, tumor dose	At 74 mo. patient "saw large print at 5 ft." At 8 yr. vision worse. At 160 mo. LMD stated patient's vision good	160 mo. Excellent
45	A. T. First series	35	F	Failing vision for 1½ yr.; amenorrhea 6 yr.; bitemporal hemianopsia; enlarged sella	Chromophobe cystic	July 1937, 3,337 r in 27 days, tumor dose. Nov. 1937, cystic tumor removed surgically	Worse after irradiation; much improved 37 mo. postoperatively	41 mo. Poor
46	G. T. Second series	28	F	Acromegaly, changed facial expression; large hands and feet; amenorrhea for 3 yr.; facial neuralgia	Acidophilic	May, 1942, 8,000 r in 27 days. Tumor dose 3,397 r	Fields improved, then decreased. Can sew and do housework; facial pains	46 mo. Poor
47	L. W. Second series	56	F	Painless failing vision for 4 yr.; bitemporal hemianopsia	Chromophobe	April 1942, 8,000 r in 24 days. Tumor dose 2,472 r	Od better; os worse. Cataracts, but otherwise all right	49 mo. Good
48	H. W. Second series	63	F	Bitemporal hemianopsia	Chromo phobe	Oct. 1940, 8,600 r in 25 days. Tumor dose 2,660 r	Vision and fields better; then constricted; operated 6 mo. post-irradiation; large pituitary adenoma found; chromophobe; scarring due apparently to x-ray; general condition good	66 mo. Poor
49	F. Y. First series	54	M	Diplopia for 4 mo.; ptosis for 2 mo.; lesion of 3rd and 4th cranial nerves; ophthalmoplegia; markedly enlarged sella; visual fields contracted	Chromophobe	March 1932, 4,277 r in 23 days, tumor dose	Fields normal in 1 yr.; post-irradiation recalcification of sella in its enlarged form; 8 yr., and 9 mo. after treatment visual fields normal	170 mo. Excellent
50	I. Z. Second series	64	F	Headaches; erosion of sella; visual fields constricted	Chromophobe	Oct. 1946, 2,385 r in 23 days, tumor dose	Loss of headaches; increased visual fields	9 mo. Excellent

irradiation. The relationship was not clear, however.

Mental Deterioration. In our report of 1941, on the treatment of 25 cases of pituitary adenomas, Cooper and I expressed the thought that in a patient with hypertension we may have caused mental deterioration through a combination of vascular and radiation damage. Even before treatment, however, this patient had had vomiting, numbness of the left ear and loss of hearing on the same side. In discussing the paper, Sosman disagreed with our conclusion on the point and voiced the conviction that with our dosage (which was higher then than now) we could not have caused cerebral damage. Along this line I have 4 more cases that I wish to discuss briefly. Two patients with symptoms of pituitary tumor were sent to us for treatment from psychopathic hospitals. In each instance there was some increased mental lucidity and questionable improvement of vision immediately following treatment. A short time later, however, both patients relapsed into their former states of psychosis. The results have been considered poor although it is obvious that there was not much of a chance for a good result to begin with. They are not included in the reported series. A third patient (K. S.), aged fifty-one, was sent to us diagnosed as a case of chromophobic adenoma with optic atrophy and almost complete blindness. Six months following a full course of treatment, she was still blind and merely vegetative. The fourth case (V. B.) is one regarding which I am uncertain. The diagnosis had been missed on this patient for fourteen years and when we saw her, she had a spastic paraplegia, bitemporal hemianopsia and cardiac enlargement. She was given a tumor dose of 2,690 roentgens in the usual way and subjectively was much improved, both in general and as regards her vision. Eight days later, however, she became confused and complained of headaches. Symptoms suggested internal hydrocephalus and the spinal fluid pressure was 270 mm. Her temperature reached 105° F. before it subsided. She died six days later.

The whole question of damage following irradiation for pituitary adenomas seems to be bound up with the sequential factor. If treatment has been given and cerebral symptoms ensue, we (and particularly the referring department and our other medical friends) are likely to explain all phenomena as caused by the treatment. That this is not fair, we will all agree but it is difficult to avoid. These symptoms are not seen in cases of intensive irradiation of brain tumors, where more treatment is given. Also in 2 cases to whom we gave intensive irradiation for pituitary tumor who finally came to autopsy, there was no histopathologic evidence of damage to the vascular structures nor to the glial tissue. Although I am not convinced that we do not cause some damage at times, we still have no definite proof that we do. Age, sex, dosage, duration of symptoms, type of tumor, etc., seemed to have no bearing on this reaction.

Three of our cases are of considerable interest because they died and came to autopsy. The first case (R. H.) was a male, aged fifty, who was given a tumor dose of 2,990 roentgens for a chromophobic adenoma of the pituitary in September, 1939. He had bitemporal visual field cuts and an enlarged sella with headaches. During the treatment, he had further constriction of the fields but within a month he had shown great improvement. From that time on his vision improved and his headaches disappeared. In March, 1944, the patient entered the University Hospitals with pneumonia and died. Autopsy showed the pituitary fossa filled with a thick creamy hemorrhagic material which apparently represented degenerated pituitary tumor. The interesting feature was the microscopic examination which showed compressed but normal pituitary tissue. Adjacent to it and apparently causing the pressure was adenomatous tissue which showed no signs of having been irradiated.

The second case was a woman, aged

sixty-four, on whom a diagnosis of chromophobic adenoma was made and 2,660 roentgens given to the pituitary. She had some immediate response in the form of increased visual fields but there was further constriction at the end of six months and she was operated on. A tumor was found lying largely above the sella and displacing the chiasm upward and the optic nerves outward. The tumor was solid but the contents were evacuated and part of the capsule was removed. Microscopically the tumor was highly cellular and appeared viable.

The third case was a woman, aged fifty-eight, whose pituitary was given 3,672 roentgens on the basis of a diagnosis of chromophobic adenoma in February, 1941. For twenty-nine months she was in good condition and she had had improvement in her vision up to 6/6-1 in her left eye. The right had been practically blind for about a year before coming to the hospital. After more than five years following irradiation she became bedridden and was re-admitted to the hospital where she died in about two weeks with all the signs of hypothalamic irritation. At autopsy, a tumor of the pituitary, 2 cm. in diameter, was found with erosion of the posterior clinoids and pressure posteriorly. The neurologist and the pathologist considered that she had died primarily of the pituitary tumor. Microscopically, the mass was composed of apparently normal and viable tumor cells. This is the only case we have found who did well for such a long time and then relapsed.

I find it difficult to explain why some pituitary adenomas respond well to relatively small doses of radiation and why others resist large doses, but as radiologists, we are accustomed to see this in other types of neoplasm, for example, carcinoma of the lip and cervix. We accept this as being due to the radiosensitivity or radioresistance of the tissue, whatever that may mean. I find it more difficult, however, to explain why a tumor that has been irradiated and obviously influenced by the treatment (because the patient has been symptom free for years) still shows no microscopic evidence of having been treated but continues to appear entirely viable unless it be loss of turgescence and swelling.

The follow-up of the cases treated at least six years ago showed no case of excellent or good result that retrogressed and one reported as poor at ninety-six months has now an excellent result at 161 months. The case observed longest with an excellent result was seen first in March, 1932. In general, therefore, it seems fair to assume that satisfactory results are permanent although we have seen one exception to that statement.

SUMMARY

1. Review of results of irradiation of a series of twenty-four cases of pituitary tumors studied six years ago indicates that they are permanent.

2. A review of a series of fifty cases emphasizes that irradiation is a satisfactory primary method of treatment. The over-all good results are in the range of 70 per cent and the chromophobic tumors respond as well as the acidophilic.

3. It is important to follow the results of treatment carefully for at least two months, particularly regarding the visual fields. If there is diminution of the fields at that time, the neurosurgeon should be called in consultation because the tumor is either cystic or otherwise radioresistant.

4. Psychotic patients or patients with any previous cerebral symptoms will probably not do well and may have their symptoms exaggerated. It is questionable whether they should be irradiated.

5. Our experience indicates that there may possibly be occasional cerebral damage from irradiation although of this there is no proof. The evidence is sequential.

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DISCUSSION

DR. MERRILL C. SOSMAN, Boston, Mass. I think we can all agree with everything that Dr. Kerr has presented this morning, and agree with his conclusions that irradiation has a beneficial effect on the majority of pituitary adenomas.

I would like to point out that this is a long-range project. A five year survival means nothing in this type of patient with this type of tumor, as it does in the malignant tumors we are more accustomed to dealing with. It is really a long-range project, and I hope that Dr. Kerr will again present these same patients and their follow-up ten years from now, with additional cases that may accumulate in the meantime.

There are three points that I want to emphasize. One is that I think we can say there is conclusive proof that irradiation has a beneficial effect on 70 to 80 per cent of the pituitary adenomas, and that the beneficial effect persists in the great majority of those so treated.

Second, that roentgen therapy, particularly in the earlier days, was not without danger and damage. When I started in 1922, we were using low voltage technique, a rather thin filter, and we customarily gave repeated doses several weeks or months apart in following these patients. We have found 7 or 8 cases of what Dr. Camp called "irradiation necrosis" of the bone in patients coming back fifteen or twenty years after the original treatments were given. I shall show you an example of one of those patients.

The exact dose to be given and the exact method of giving it is still subject to discussion. I am inclined to believe from the evidence presented that Dr. Kerr has a much better method at present than we had twenty-five years ago. We have gradually been moving toward the same conclusion that Dr. Kerr has reached.

There is one thing we must avoid, which is a very common failing among radiologists: the conclusion that if a certain dose gives a good result, an increased dose must necessarily give a better result. That is an entirely erroneous conclusion, and I am afraid it is a form of wishful thinking which is all too prevalent in our profession. I have been guilty of the same sort of erroneous deduction myself.

The third thing is that these tumors often

spontaneously tend toward a burned-out stage of hypopituitarism, particularly the acidophilic tumor. The end stage of hypopituitarism has been rather hopeless, as far as treatment goes, up to the present time. The patient appears quite similar to a patient with myxedema: sluggish, somnolent, with very little activity, but thyroid even in large doses has no effect on these patients with hypopituitarism. Dr. Thorn at our hospital has been using adreno-corticotropic hormone, extracted from pituitary glands (A.C.T.H.) which alleviates many of these symptoms if the patient's adrenal glands are intact.

(Dr. Sosman then showed several slides, first illustrating the skin atrophy and telangiectasia in the temporal areas which resulted from the earlier low voltage irradiation, and the underlying mottled absorption of the temporal bones which increased in extent and degree as the years elapsed. Then he showed tables and charts of Dr. Thorn's work in replacement therapy of pituitary deficiency by the adreno-corticotropic hormone (A.C.T.H.) The details will be found in the Holmes Lecture and in the Caldwell Lecture which are to appear later in this JOURNAL.)

In conclusion, I would like to congratulate Dr. Kerr on his excellent presentation and hope that he will follow this group of patients as long as he can. When patients have relatively benign tumors such as pituitary adenomas, it is often a question whether or not the doctor will survive his patient.

THE GASTROSCOPIC PICTURE IN POST-IRRADIATION GASTRITIS*

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BRICK[1] in 1946 described the new post-therapeutic clinical entity of chronic gastritis following massive irradiation to the upper abdomen. He has presented data on the clinical, roentgenographic, and pathologic aspects of post-irradiation gastritis in a series of soldiers who had been treated for metastatic malignancy.[1,2]

The present communication deals with the gastroscopic picture presented by the group of patients from which Brick drew his material. Since other aspects of post-irradiation gastritis have already been adequately described by Brick, an attempt has been made to include here only material which has a direct bearing on the gastroscopic findings.

MATERIALS AND METHODS

The 12 patients considered were soldiers who had been diagnosed and treated for malignant conditions while in the service. All were white males, aged twenty to thirty-three. The diagnosis in each case had been made by histopathologic study. One had a retroperitoneal reticulum cell sarcoma, 4 had seminoma of the testis, 3 had malignant teratoma of the testis, and 4 had embryonal carcinoma of the testis. Surgical procedures in various patients had included orchidectomy, radical parailiac and paraaortic node resection, exploratory laparotomy, and gastric resection, the last for perforation and hemorrhage complicating post-irradiation gastritis.

Radiation therapy had been given with the 1,000 kilovolt machine through five portals which had been constant in size and position in all patients.† The gastric area was involved by two of these portals: a 10 by 10 cm. epigastric portal, the inferior border of which had been placed 25 cm. above the base of the penis, and a 10 by 15 cm. lumbodorsal portal along the long axis of the spine and centered over the second lumbar vertebra. The radiation doses given here are expressed in terms of skin dosage.

The gastroscopic examinations were made by one observer. The Cameron-Schindler omniangle instrument was used. Pre-examination medication consisted of a retention enema of 0.4 gm. nembutal one to two hours beforehand and atropine 0.0008 gm. subcutaneously one-half to one hour beforehand.

The gastroscopic findings described below are taken directly from the original reports. To save space, references to the normal appearing portions of the stomach and statements of negative findings are for the most part omitted. In each case, at least the proximal half of the stomach—the part which was outside of the field of radiation—was normal, and in many only the distal third showed pathologic changes. In no case did preliminary drainage of the stomach bring up a significant amount of blood; in 10 of the 26 drainages the fasting contents contained free acid.

In the cases of those patients who came to gastric resection, the pathologic pictures presented by the resected specimens are outlined. The findings at upper gastrointestinal roentgenography are also presented when they were done within thirty days of gastroscopy.

CASE PRESENTATIONS

In the presentations below, the date of each examination is expressed in terms of

† Physical factors: 1,000 kv. Total filtration 3 W., half-value layer, 3.6 mm. Pb., 3 ma., 70 cm. distance, 80 r per minute, measured in air.

* Grateful appreciation is extended to the Photographic Laboratory, Walter Reed General Hospital, for the reproductions of the illustrations.

days following the last day of radiation treatment.

Case I. Twenty-nine years old. Seminoma of the testis. Treatment: 12,600 roentgens over a thirty day period; 2,400 r to epigastric portal and 2,400 r to lumbodorsal portal.

Gastroscopy, thirty-six days: "The whole pars media shows paleness and increased translucency, plus total absence of rugae, suggestive of edema. The fundus is normal without abnormal mucosal or rugal change. The antral configuration is normal, but this portion distends poorly with air, and its walls, although of normal color, appear thickened. The pylorus is well visualized and is seen to close regularly with shallow antral peristalsis; there is no bile reflux. On the greater curvature of the antrum, just distal to the anterior end of the angulus, there is a rather deep, clean, elliptical ulcer three rugal widths in length and two rugal widths in breadth. The long axis of the ulcer runs obliquely anteroposteriorly. The base is gray, homogeneous and clean. There is no exudate or bleeding, and the margins show almost no inflammatory reaction. There is no nodularity."

Gastrointestinal roentgen series, forty-two days: Normal, with normal mucosal pattern, except for narrowing of the antrum.

Gastrointestinal roentgen series, sixty-two days: Normal.

Gastroscopy, seventy-nine days: "The ulcer previously seen is now almost circular in outline. It is likely that this change in shape is due to healing, for there appears to have been some reduction in size. Again it is noted that there is practically no inflammatory reaction of the ulcer margin and no contraction or other evidence of fibrotic change at its base. The base is gray and clean and there is no exudate, bleeding or nodularity. Its depth is still as great as its width. The pylorus is normal anatomically and functionally, but antral peristalsis is shallow and infrequent. At this time there is no edema or apparent infiltration of the distal portion of the stomach. The rugae of the greater curvature now appear normal, and they pass by the ulcer site without distortion."

Gastroscopy, ninety-five days: "The appearance of the ulcer has changed, but its size probably has not. At this time there is evidence of inflammatory reaction at the periphery with a narrow margin of intense hyperemia and edema. These changes probably account for the apparent increase in the ulcer's depth. An interesting picture is presented in that the rugae pass by the ulcer without distortion. Although peristalsis is minimal, there is no sense of generalized infiltration of the walls of the distal stomach. Pylorus is normal."

Gastroscopy, 143 days: "The site of the former ulcer is now occupied by a small white circular scar; there is no evidence of contracture at the scar and the paths of the rugae of the region are not distorted. Again there is no impression of rigidity or infiltration of the gastric walls. The peristalses at this time are unimpeded, and the antrum and pylorus are normal anatomically and functionally. There is much thick, yellow-gray mucus on the posterior wall."

Gastroscopy, 209 days: "The scar is now almost indistinguishable from the surrounding mucosa, showing only a pink saucerization. The rugae of the region are not distorted or deformed. There is no functional impairment. This is an essentially normal stomach."

Case II. Thirty years old. Embryonal carcinoma of testis. Treatment: 25,800 roentgens over seventy-five day period; 5,400 r to epigastric portal and 4,800 r to lumbodorsal portal.

Gastroscopy, 192 days: "The pylorus is well visualized and is seen to function normally, responding to regular antral peristalses. The antrum shows no rigidity and dilates easily on inflation. The rugae everywhere are normal and iron out well. There are no evidences of infiltration of the stomach wall, and no generalized mucosal abnormalities are present. The mucous lake is largely bile. On the greater curvature of the antrum, midway between the pylorus and the angulus, there is a clean, punched-out, rather deep elliptical ulcer. The ulcer runs obliquely anteroposteriorly across the greater curvature. Its length is equal to about four rugal widths and its breadth to about two. The base is gray and clean without exudate, bleeding or nodularity. The periphery of the ulcer shows no hyperemia or infiltration. The mucosa is normal up to the crater margin. There is only a minimal suggestion of contracture of the site as judged by mucosal radiations. The rest of the stomach appears normal in all respects."

Case III. Twenty-six years old. Malignant teratoma of testis. Treatment: 23,900 roentgens over forty-nine day period; 4,800 r to epigastric and 4,800 r to lumbodorsal portals.

Gastroscopy, 197 days (Fig. 1): "The mucosa

is pale. There is a bubbling bile reflux through the constantly patulous pylorus. The antrum is tubular and distorted, and cannot be distended by inflation. Its configuration is such that the entire circumference is visualized. The distal half of the pars media is stiff. The entire distal half of the stomach shows marked generalized submucosal infiltration which apparently is responsible for the stiffness, distortion and failure of the antrum to inflate. Rugae here are absent. The mucosa of the region is more

FIG. 2. CASE V. Two hundred and thirty-nine days after completion of radiation therapy.

than usually translucent, with increased highlights. There is no ulceration, erosion, petechia, free blood, or atrophic or hypertrophic gastritic change. The proximal half of the stomach is normal."

CASE IV. Thirty-three years old. Seminoma of testis. Treatment: 24,700 roentgens over seventy-six period; 4,900 r to umbilical portal and 5,000 r to lumbodorsal portal.

Gastrointestinal roentgen series, 276 days: There is narrowing and fixation of the prepyloric area. The stomach is inactive.

Gastroscopy, 284 days: "The motility of the distal half of the stomach is markedly impaired and peristalsis was not observed in the antrum over a period of several minutes. The antrum shows marked submucosal infiltration which gives this region a tubular appearance; the angulus is involved in the process and is not prominent. The pylorus appears normal but remains in a partially contracted state, and was not seen to relax or to close during the examination. There is a small amount of bile regurgitation. The mucosa everywhere is intact without ulceration. There are many superficial petechiae scattered over the greater curvature of the distal pars media."

CASE V. Twenty years old. Embryonal carcinoma of the testis. Treatment: 24,000 roentgens over sixty-one day period; 4,800 r to epigastric portal and 4,800 r to lumbodorsal portal.

Gastrointestinal roentgen series, 133 days: "There is a deep crater on the anterior wall. The mucosa and peristalsis are normal except for the area of the ulcer."

Gastroscopy, 147 days: "The distal third of the stomach is a stiff contracted tube lined with closely pressed rugae which cannot be effaced because the region fails to distend on inflation. No peristalsis is seen. The pylorus is not visualized. On the mid-anterior wall of the pars media there is a deep elliptical ulcer, estimated to be 2.5 by 1 cm. in diameter. The floor is covered by a dirty gray membrane and the edges are a little elevated. There is no hyperemia, bleeding, nodularity or contracture at the site."

Gastroscopy, 238 days: "Examination is rather unsatisfactory because of rapid passage of air through the stiff fixed tubular antrum. The pylorus is not seen but is presumed to be constantly patulous because of the quick deflation and collapse of the proximal stomach. The region of the angulus at this time appears normal, the infiltration now being limited to the antrum. There is considerable thick, gray mucus scattered about. No ulceration, scar or other localized mucosal lesion is seen."

Gastrointestinal roentgen series, 239 days (Fig. 2): "The stomach is small and shortened on its lesser curvature side. The antral mucosa is denuded. The antrum is rigid, decreased in caliber and fixed. There is an ulcer 2 cm. in diameter on the posterior wall of the antrum. The pylorus is open. Peristalsis is extremely sluggish."

Gastroscopy, 293 days: "Although peristalsis is very weak and infrequent through the antrum, the pylorus is now normal both anatomically and functionally. The antrum is narrow and distorted, pointing inferiorly and

FIG. 1. Case III. One hundred and ninety-seven days after completion of radiation therapy. Tubular distortion of antrum by submucosal infiltration, allowing visualization of all sides. Absence of rugae. Fixed patulous pylorus with bile reflux.

FIG. 4. Case VIII. Six hundred and eighteen days after radiation therapy. Thick yellow-gray mucus. "Tight" angulus. Submucosal infiltration.

FIG. 3. Case VII. Five hundred and seventy-one days after radiation therapy. Tubular infiltrated antrum. "Tight" angulus. Large petechiae.

posteriorly. On the lesser curvature of the antrum there is a punched-out circular ulcer, about four rugal widths in diameter. The base is gray and clean without bleeding or exudate. The periphery is involved in a mild generalized hyperemia which is seen in the mucosa of most of the distal half of the stomach. On the anterior wall of the pars media and on the lesser curvature just proximal to the angulus there are small superficial erosions which are not bleeding. Scattered about the antrum and distal pars media there are about ten minute flame-shaped petechiae. No evidence of the previously seen anterior wall ulcer is found."

Gastrointestinal roentgen series, 297 days: "Distal half of the stomach is rigid with markedly decreased caliber. It is shortened at its lesser curvature. Peristalsis is sluggish. There is an ulcer 2 cm. in diameter on the posterior wall of the proximal antrum on the lesser curvature side."

Gastroscopy, 353 days: "The antrum points posteriorly but, although distorted, it appears normal in circumference and dilates satisfactorily on inflation. The pylorus appears normal as does antral peristalsis. The lesser antral curvature cannot be seen and no opinion can be given regarding the site of the previously described antral ulcer. The anterior wall of the pars media is satisfactorily visualized and there is no residual change to demarcate the site of the large ulcer formerly found in this area. There are three small pigmented spots in the greater curvature of the pre-antral region, but no petechiae or erosions."

Case vi. Thirty-three years old. Reticulum cell sarcoma, retroperitoneal. Treatment: 7,400 roentgens over fifty-five day period; 3,600 r to epigastric portal and 3,800 r to lumbodorsal portal.

Gastrointestinal roentgen series, 327 days: "There is hypomotility of the distal half of the stomach and hypertrophy of the rugae."

Gastroscopy, 329 days: "The interior configuration of the stomach and the consistency of the gastric walls are normal. There is no evidence of fixation, infiltration or generalized mucosal change. The pylorus is normal anatomically, but remained patulous without closing while under visualization for several minutes. The mucosa everywhere is normal except for a shiny white circular scar 1 by 1 cm. at the middle of the angulus margin."

Gastroscopy 336 days after therapy was normal except for the persistent patulousness of the pylorus and the previously described scar on the angulus.

Gastroscopy 377 days after therapy showed no change. The infrequency of antral peristalsis was notable, as was the constant bile reflux.

Case vii. Twenty-nine years old. Embryonal carcinoma of the testis. Treatment: 15,000 roentgens over ninety-eight day period; 5,400 r to epigastric portal and 4,800 r to lumbodorsal portal.

Gastroscopy, 571 days (Fig. 3): "Preliminary drainage of the stomach brought up about 300 cc. of poorly digested food from the previous day. In spite of lavage, a large portion of the fundus was obscured by retained material. The antrum is tubular and narrow with heavy submucosal infiltration. Although the infiltration seems to stop distal to the angulus, the latter appears 'tight' and does not expand on inflation of the stomach. The angulus is, however, thin with normal appearing mucosa. The pylorus was not well seen. There is no bile reflux. Scattered over the pre-antral region are many dark red petechiae of varying size, the largest being about two rugal widths in diameter. Among the petechiae there are a few dark brown pigmented spots. The mucosa elsewhere is normal but pale, without ulceration or erosion."

Gastroscopy, 585 days: "There was a moderately large mucous lake, but except for this area and the pylorus, all levels were well visualized. The interior configuration of the antrum is considerably distorted, with narrowing and fixation. The pylorus again remained obscured by the 'tight' angulus. The infiltration through the antrum is marked. No peristaltic motion whatever is seen. The petechiae and pigment spots appear as before. No bile reflux. No ulceration."

Case viii. Twenty-eight years old. Seminoma of testis. Treatment: 25,000 roentgens over fifty-three day period; 5,000 r to epigastric portal and 5,000 r to lumbodorsal portal.

Gastrointestinal roentgen series, 603 days: "The stomach is small and shortened on its lesser curvature. The antrum is constricted, canalized and fixed. The mucosa of the corpus and antrum is atrophic. The pylorus is open."

Gastroscopy, 613 days: "The examination is not satisfactory because most of the mucosa is obscured by a rather uniform coating of thin, yellow-gray mucus. The antrum is decreased in

caliber and so fixed that it could not be at all dilated by inflation. No peristalsis is noted in the stomach. The pylorus was constantly obscured by the angulus. Because of the mucus, no opinion can be given regarding the appearance of the mucosa."

Gastroscopy, 618 days (Fig. 4): "All levels were well visualized except for the distal antrum which remained in the shadow of the 'tight' angulus and a portion of the fundus which was obscured by a rather large bile lake. No peristaltic motion was seen in the stomach. At this time there are only a few patches of yellow-gray mucus scattered about. The antrum is decreased in diameter and appears thickly infiltrated, failing to expand on inflation. The rest of the mucosa is normal. On the posterior wall of the pars media close to the greater curvature there is a small bulge without distortion of the rugae; this gives the impression of an extrinsic mass pressing on the stomach wall."

Gastroscopy, 633 days: "The pylorus again is not visualized but its patency is assured by the constant reflux of frothy bile. No peristalsis is seen. The antrum is rigid and tubular, showing infiltration of its walls. The mucosa everywhere is intact and of normal color. Proximal to the antrum there is no infiltration or fixation."

Fig. 5. Case ix. Ninety-one days after radiation therapy.

Case ix. Twenty-two years old. Malignant teratoma of the testis. Treatment: 24,000 roentgens over fifty-four day period; 4,800 r to epigastric portal and 4,800 r to lumbodorsal portal.

Gastrointestinal roentgen series, ninety-one days (Fig. 5): "The stomach is contracted and shows a bulge on the greater curvature of the antrum which simulates an ulcer. The stomach is rigid and there is no peristalsis. The mucosa is granular and hypertrophied."

Gastroscopy, ninety-nine days: "The greater curvature of the antrum is obscured by regurgitated bile, but the examination is otherwise satisfactory. The antrum is stiff and elongated, and no motion is seen in the region, either as result of peristalsis or inflation of the stomach. The pylorus is well seen at the end of the tubular antrum and remains patulous. There is intermittent bile reflux. The submucosal infiltration stops about 1 cm. proximal to the angulus, the transition to normal thin mucosa being rather abrupt. The angulus is blunt and heavy. No mucosal lesion per se is found."

Gastrectomy, 224 days. Pathologic report: "The mucosal surface is markedly edematous and hyperemic, with punctate hemorrhages scattered over the surface. The rugae are ironed out as the pylorus is approached, and 2.5 cm. from the pylorus is an irregular, ulcerated area, measuring 0.3–1.5 by 2–4 cm. The ulcer is up to 3 mm. deep. The base is gray-pink friable tissue, covered with fibrin. The serosal surface is somewhat dull and has a leathery feel. Microscopic: The base of the ulcer is covered by fibrinous exudate, beneath which is a narrow zone of granulation tissue infiltrated by a subacute inflammatory reaction. The edge of the ulcer shows gradual thinning of the mucosa and glands with a marked submucosal subacute inflammatory reaction. The submucosa shows rather severe interstitial edema, and there are focal areas of subacute inflammatory infiltrate in the serosa."

Case x. Twenty-five years old. Malignant teratoma of the testis. Treatment: 26,000 roentgens over fifty-five day period; 5,200 r to epigastric portal and 5,200 r to lumbodorsal portal.

Gastroscopy, 130 days: "The antrum is directed superiorly and anteriorly, and probably not more than half its length is visualized. The angulus and musculus sphincter antri are large and thick with tightly stretched mucosa. This infiltration extends into the antrum as far as visualization can be carried, and the resulting

fixation seems responsible for the inability of the distal half of the stomach to expand on inflation."

Gastrointestinal roentgen series, 148 days (Fig. 6): "The antrum is narrow and the rugal pattern is distorted. The pylorus remained patent throughout the examination. The rugae everywhere are considerably hypertrophied."

Gastrectomy, 190 days. Pathologic report: "In the prepyloric region the stomach wall is 1.5 cm. thick. The serosal surface is smooth and glistening. The mucosa is greatly thickened and extremely edematous, as are the tissues beneath it. The convolutions are soft and velvety, showing petechial hemorrhages. In the pyloric canal there is an ulcer 1.8 by 1.7 cm. in diameter and 0.6 cm. deep. Microscopic: There is widespread edema with considerable loose submucosal fibrosis and associated marked chronic inflammation. The muscularis shows edema with areas of chronic inflammation. The mucosa shows marked metaplasia to an intestinal type of epithelium, with many glands lined by goblet cells. The glands are for the most part moderately atrophic. There is a mild increase in fibrous tissue between the glands. The ulcer surface is covered by fibrous tissue with deep fibrosis below the ulcer."

Gastroscopy, 355 days: "The distal portion of the stomach has been resected and now the interior configuration is almost spherical. The enterostomy stoma is close to the greater curvature and appears adequate in size. Very little of the jejunum is seen. The stomal margin appears healthy without ulceration. Several rugal crests are hyperemic, but, except for this, there is no erosion, infiltration, petechia, atrophy, hypertrophy or other abnormal mucosal change."

Case xi. Twenty-nine years old. Embryonal carcinoma of testis. Treatment: 13,000 roentgens; 5,500 r to epigastric portal and 5,500 r to lumbodorsal portal.

Gastroscopy, 150 days: "The usual 'tube-like' appearance is seen, constituting the distal third of the stomach. The angulus is apparently severely involved in this infiltration process and is not recognizable as such. Inflation does not change the appearance of the distal stomach. Air quickly passes through the presumably patulous pylorus, although the latter is not seen. When the stomach deflates and the lateral walls collapse around the objective, the antral lumen remains tubular and patent. No mucosal lesions are found."

Fig. 6. Case x. One hundred and forty-eight days after radiation therapy.

Gastrointestinal roentgen series, 166 days: "There is marked narrowing of the stomach extending from the lower portion of the pars media through the antrum. There is an ulcer crater measuring 2 by 5 mm. on the greater curvature 3 cm. proximal to the pylorus."

Gastrectomy, 190 days. Pathologic report: "The serosa is smooth except for a 3.5 by 1.3 cm. area with shaggy tags. The mucosa shows normal rugae over the proximal 2.5 cm. of the specimen, and here the wall is 0.8 cm. thick. Distally there is great thickening of all layers with a spongy edematous feeling on palpation. There is much submucosal brown-red hemorrhage near the junction of the middle and distal thirds. Microscopically the mucosa shows multiple areas of superficial hemorrhage. The submucosa is considerably thickened and replaced by hyaline material. Throughout this layer there are loosely arranged coarse collagenous fibers producing rather marked fibrosis. The muscle shows areas of edema plus occasional areas of fibrosis. There is a minimal chronic gastritis with moderate atrophy and intestinal metaplasia af the mucosa."

Gastroscopy, 365 days: "The distal stomach has been resected. On the posterior wall at the distal end near the greater curvature, there is an enterostomy stoma, through which there is bile reflux. The size of the stoma appears adequate, and its edges, which were only seen briefly before the reflux began, appear healthy without ulceration or free suture. Everywhere the mucosa appears normal. There is no evidence of infiltration or sense of stiffness."

Gastrointestinal roentgen series, 367 days: "Normal posterior gastroenterostomy without evidence of stomal ulcer."

CASE XII. Twenty-seven years old. Embryonal carcinoma of the testis. Treatment: 22,400 roentgens over fifty day period; 5,600 r to epigastric portal and 5,600 r to lumbodorsal portal.

Gastroscopy, 345 days: "Although the antrum is immobile, there is no evidence of infiltration. The pylorus is normal functionally and anatomically, and a peculiar picture is presented by the rhythmic contractions of the pylorus since there is no peristalsis in the antrum itself. The mucosa is normal in all respects except for several deep pigmented spots scattered along the greater curvature."

DISCUSSION

It is clear that only those areas of the stomach which had been directly in the path of roentgen irradiation showed changes demonstrable by endoscopy. It is also clear that the size of the radiation dose was not the only factor determining the degree of subsequent gastric damage, suggesting individual variation in irradiation tolerance which precluded accurate prediction of the gastroscopic picture in any particular patient. This is not to say that experience with this group of patients has failed to indicate a satisfactory maximum safe dosage; in fact, the Radiation Therapy Section at this hospital has succeeded in balancing the minimum effective dose against the maximum safe dose so effectively that the Gastrointestinal Section does not expect to see more post-irradiation gastritis.

The most characteristic part of the endoscopic picture was heavy submucosal infiltration of the involved area, with consequent stiffening and fixation of the gastric walls. In the antrum this led to a tubular deformity which neither expanded on inflation nor collapsed after instilled air had passed through the stomach. It was interesting to note that this infiltration did not occlude the pyloric canal; rather, the pylorus typically remained patulous, as though there was paralysis of the sphincter musculature, allowing an unusual amount of bile reflux and often interfering with maintenance of satisfactory gastric inflation. As would be expected, submucosal infiltration was attended by notable sluggishness or absence of antral peristalsis. But poor peristalsis was also found in post-irradiation stomachs which showed no infiltration or fixation, a finding which suggests that it was radiation injury to the local neuromuscular mechanism rather than mere mechanical interference which interrupted motility. It is recognized, of course, that accurate gastroscopic interpretation of gastric motility is probably seldom possible, especially in view of large doses of pre-examination atropine, but some opinion regarding this aspect of the gastric situation is almost always possible. Statements concerning motility in the case reports are felt to be valid.

Of mucosal lesions, deep clean-cut ulceration was most important. In one case the course of an ulcer was closely followed, and its complete healing without residual contraction or distortion was eventually seen. This and the slowness of healing were features which differentiated the radiation ulcer from simple peptic ulcer. It was a matter of considerable surprise to find at gastroscopy no residual abnormality to indicate the site of an ulcer estimated at 2.5 by 1 cm. in diameter visualized three months previously.

The chronicity of the observed mucosal and submucosal damage in several of the cases was an important feature. At the onset of the study it was wondered if the ulcers would heal spontaneously in view of the fact that some were followed several months without change. In other cases the ulcers first appeared many months after the completion of irradiation. Because the swelling of the antral submucosa likewise was found as long as a year and a half following treatment, it was interpreted erroneously as being due to chronic infiltration. The static nature of this localized edema for long periods is not easily explained.

Petechiae, pigmentation and excess mucus were common but not distinctive features of the mucosal changes. Paleness reflected the anemia of some of the patients.

Examinations following subtotal gastric resection with enterostomy showed the usual picture of postoperative stomach with no feature to indicate the prior post-irradiation changes, nor were stomal ulcers or significant postoperative gastritic changes found. In each case the damaged portion of the stomach had been completely resected, and the final results were satisfactory clinically and endoscopically.

The correlation between the gastroscopic picture and the pathology of the resected specimens was fairly satisfactory. That which was taken for submucosal infiltration, however, proved to be mere edema. In addition, the large amount of fibrosis underlying the post-irradiation ulcer was an unexpected finding in view of the remarkable absence of contracture about the healing ulcer, gastroscopically observed.

When the gastroscopic findings are compared with the roentgen findings, the only important discrepancy is seen to be that of detection of ulcer. Each method brought to light such lesions not visualized by the other. Specific comparisons are not important here, but it was found that the ulcers missed by gastroscopy were those which were hidden in narrow distorted antrums.

The diagnosis of post-irradiation gastritis has been, of course, no problem, nor should it ever be. The entity should disappear as a result of the present experience. There is hardly need for a differential diagnosis, but one notes that in a case of luetic gastritis Carey and Ylvisaker[3] have described a gastroscopic picture similar to that of post-irradiation gastritis.

SUMMARY

Gastroscopic studies in twelve patients who had developed post-irradiation gastritis following intensive radiation treatment for malignant disease showed remarkably constant and characteristic gastric changes. The picture included marked edema with tubular deformity and fixation of the antrum, similar fixed patulousness of the pylorus, and clean deep chronic ulcers which healed without contracture. Following subtotal gastrectomy with posterior gastroenterostomy, the picture was that of normal postoperative stomach. Pathologic and roentgenographic studies in general corroborated the gastroscopic findings. A new gastroscopic entity is presented, but, because the diagnosis of post-irradiation gastritis should be obvious from the history, the importance of endoscopy lies in the evaluation of the severity of the radiation damage.

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CANCER OF THE CERVIX UTERI*

A REVIEW OF 296 CASES, 1935–1944

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THIS report consists of an analysis of 296 consecutive cases of cancer of the cervix uteri, registered in the tumor clinic of a general hospital from 1935 to 1944, inclusive, with particular reference to methods of treatment and end results. The renewed interest in the radical Wertheim operation as the treatment of choice in selected cases makes it imperative to report the results obtainable with radiotherapy, since Meigs[5] has stated that radiation therapy is at a standstill. Many previously reported series consist of cases collected over a period of fifteen to thirty years, when methods of radiation therapy were changing rapidly. To quote the cure rates obtained in such a series is almost like quoting the surgical cures of cancer of the breast before Halsted. Other series reported, especially from large teaching clinics, represent the collective work of many individuals with very different knowledge, experience and skill. A noteworthy exception to this practice is the series of Pitts and Waterman[7,8] and Waterman and Di Leone.[12] Their results demonstrate the importance of personal, individual management of a large group of patients by technically good and relatively constant methods.

SOURCE OF MATERIAL

All patients admitted to the hospital with proved cancer of the cervix have been registered in the tumor clinic. Private, ward service and dispensary patients are included. Indigent patients are accepted for treatment. The proportion of Negro patients treated is somewhat higher (21 per cent) than that of the community (13.5 per cent). Most of these are medically indigent, indicating a slight preponderance of the less favored economic groups in our series. Survival rates among Negro and white patients are the same, indicating that they received comparable treatment (Table x).

Stage of disease has not determined the acceptability of cases for treatment, except that patients too ill to report for roentgen therapy as out-patients frequently could not receive treatment, and were subtracted from the determinate group for that reason. On occasion it was possible to admit such patients to the hospital for roentgen therapy; if treated, they are included in the determinate group, even though many never improved enough for radium therapy (22 of 208). All these are among our failures and also most of those requiring admission for preliminary roentgen therapy, even though radium could later be used.

PATHOLOGY

All cases in the determinate group had histopathologically proved cancer. Only 1 case was considered carcinoma in situ. The pathologic report in 203 cases was squamous cell carcinoma and in 5 cases was adenocarcinoma. (Cases of adenocarcinoma of the corpus uteri involving the cervix secondarily are not included.) There was no significant difference in survival rate.

INDETERMINATE CASES

This analysis is based upon a determinate group of treated cases from which conclusions can be drawn. It is necessary to define those cases to be excluded from the determinate group (Table 1). In general, the postulates laid down by Martin, Munster and Sugarbaker[3] are followed, with one im-

* Presented at the Twenty-ninth Annual Meeting, American Radium Society, Atlantic City, N. J., June 9–10, 1947.

portant exception: we do not include cases which were admitted with cancer recurrent after previous treatment elsewhere. We believe recurrent cases belong to the original treatment series of which they were a part at another clinic; that including them in our results would represent duplication of reporting. Many such recurrent cases presented themselves with a healed primary lesion for treatment of metastatic disease. Recurrent cancer might have been excluded from consideration by various methods: Many had no biopsy; many had no treatment other than terminal nursing care. We consider them indeterminate from the standpoint of analyzing the results of treatment.

TABLE I

SELECTION OF DETERMINATE CASES

	1935–1942		1935–1944	
Indeterminate		65		88
Recurrent cancer	23		33	
Untreated	31		37	
Consultation only	5		9	
Died, intercurrent disease	5		8	
Lost, well 3 years	1		1	
Determinate		156		208
Total admissions		221		296

Recurrent Cancer. A separate analysis of recurrent cancers admitted from 1935 to 1942 showed that of 32 such cases 9 received no treatment and 23 had palliative radiation therapy. The 9 untreated recurrent cancers are included with the other untreated cases in Table 1. Of 23 recurrent cases treated, 3 survived five or more years.

Untreated cases in the five year (1935–1942) series fall into three categories. Of 31 untreated cases, 10 refused treatment and presumably went elsewhere; their present condition is unknown. There were 13 cases unable to report for treatment (distance, physical condition), 3 of whom were moribund, dying one, four and fourteen days respectively after the initial examination. Eight recurrent cases could not be treated because of damage resulting from previous radiotherapy (skin atrophy, colitis, pelvic cellulitis or slough). The other recurrent case referred to above was one of those moribund on admission (liver metastasis, healed primary cancer).

Consultation only describes 5 patients who were seen in consultation while under treatment elsewhere or followed by us at the request of another clinic. Two of these patients are known to be living seven and fourteen years respectively. None of these patients were treated by us, nor included among our survivors.

Intercurrent Disease. Several patients dying from unrelated diseases cannot be considered either cures or failures of treatment. Presumably their prognosis was the same as that of the whole series and their exclusion from the determinate group should have no statistical effect. No case was excluded from the determinate group for this reason unless the cause of death was known. The 5 cases from the five year series are tabulated below, with survival time.

1. Pulmonary tuberculosis: 2 months.
2. Coronary thrombosis, ruptured ventricle: 30 months.
3. Cerebral thrombosis: 13 months.
4. Hypertensive cardiovascular disease: 34 months.
5. Carcinoma of bronchus: 39 months.

STAGE OF DISEASE

The classification of Schmitz and Nelson[9] has been used since it is practical and well correlated with the clinical course of cervical cancer. In this report Group I is defined as a small, limited cancer, apparently confined to the portio vaginalis, not over 2 cm. in diameter. Group II is a cancer involving most of the cervix (or a small endocervical cancer whose exact extent is usually greater than can be seen) but not extending beyond the cervix. Group III is a cancer invading parametrium or vagina by direct extension. Group IV is the cancer with a frozen pelvis from infiltration out to the lateral pelvic wall, or with distant metastasis, including nodules at the vaginal introitus.

The following data have been calculated in this series (Tables II, III, IV):

TABLE II

STAGE OF DISEASE AND SURVIVAL RATE
Determinate Cases
1935–1942 (5 years)

Group	I	II	III	IV	All
Alive	14	40	24	2	80
Total	16	60	57	23	156
Rate	87.5%	67%	42%	9%	51%
	1935–1944 (3 years)				
Alive	24	56	55	5	120
Total	25	81	73	29	208
Rate	96%	70%	52%	17%	57%

TABLE III

RACE AND STAGE OF DISEASE
(Including some indeterminate cases)

Group	I	II	III	IV	All
White	22	72	63	27	184
Negro	5	14	18	21	58
All cases	27	86	81	48	242

TABLE IV

DURATION OF SYMPTOMS AND STAGE OF DISEASE

Group	I	II	III	IV
White	5 mo.	7½ mo.	8 mo.	11 mo.
Negro	3 mo.	5 mo.	7 mo.	14 mo.
All	5 mo.	7 mo.	7½ mo.	12 mo.

The downward trend of survival with respect to duration of symptoms confirms the clinical classification of cases.

An analysis of those cases treated up to 1939 with respect to duration and survival for three years produced a paradoxical result. Of 33 Group II cases, 21 living patients had symptoms for an average of seven months and 12 who died, for 9½ months. On the other hand, of 41 Group III cases, the 21 survivors had symptoms for 7½ months, and 20 who died had symptoms only 5½ months—shorter average duration than the Group II cases. We conclude that this group had more highly malignant cancers, with rapid growth, greater invasion and more severe symptoms leading to earlier, yet fatally late, diagnosis and treatment (Table v).

TABLE V

STAGE OF DISEASE AND DURATION IN MONTHS WITH RESPECT TO SURVIVAL FOR 3 YEARS
1935–1939

Group	I	II	III	IV
No. of cases	10	33	41	21
Alive	3½ mo.	7	7½	*
Dead	*	9½	5½	11½
All	3½ (0–10)	8 (1–24)	6½ (0–24)	11½

* Only 1 patient in each of these categories.

CAUSES OF DELAY

The failure of the patient to seek advice after the onset of symptoms accounted for delay in diagnosis and treatment in two-thirds of the cases. Usually this was due to the patient's ignorance of the importance of unusual bleeding or discharge. For example, many patients date the onset of their illness to spontaneous vaginal bleeding; unless the specific question is asked they forget or ignore post-coital bleeding occurring weeks or months earlier. Rarely, patients defer consultation because of fear or excessive modesty.

In one-third of the cases, delay up to twelve months was due to the failure of one or more physicians to make a diagnosis. The most frequent medical errors are: hormone medication without examination, under the assumption bleeding is functional; medication to control bleeding pending future examination; treatment for some other condition such as myoma or salpingitis, cystitis or hermorrhoids; and deferral of examination "until you stop menstruating."

AGE INCIDENCE

Particular attention is called to the frequent occurrence of cervical cancer before the age of forty (Table VI). Fifteen cases (5 per cent) were from twenty to twenty-nine years of age, and another 20 per cent from

thirty to thirty-nine. We have noted that cervical cancer occurs earlier in Negroes (Table VI). The maximum incidence, of course, is in the fifth and sixth decades.

TABLE VI

AGE INCIDENCE AND RACE
(Including indeterminate cases)
1935–1944

Age	White	Negro	All
20–29	7	8	15
30–39	41	14	55
40–49	65	20	85
50–59	63	15	78
60–69	43	7	50
70–79	5	2	7
80–	3	0	3
All ages	227	66	293

TABLE VII

AGE AND STAGE OF DISEASE
(Including some indeterminate cases)
1935–1944

Age	Group I	Group II	Group III	Group IV	All Groups
20–29	2	4	2	3	11
30–39	2	24	16	3	45
40–49	9	23	22	16	70
50–59	12	14	22	15	63
60–69	2	19	17	6	44
70–79		1	1	4	6
80–		1	1		2
All ages	27	86	81	47	241

Age apparently has some influence on the survival rate. It is our impression that very young patients (twenty to twenty-nine years) do well, but there are too few to be statistically significant, and that patients nearing the menopause do poorly. An analysis of the Group II and III cases for correlation between age and survival suggests that postmenopausal patients do better than those under fifty (Table VIII). Group I and IV cases were not tabulated by age, since 95 per cent of the former survive and 85 per cent of the latter die.

CANCER AFTER HYSTERECTOMY

There were 11 cases of cancer of the cervix after previous hysterectomy for other conditions among the 208 patients studied. The number is too small to analyze, except to state that there was no apparent effect on survival rate. Seven of these 11 cases lived three or more years (64 per cent).

TABLE VIII

AGE AND SURVIVAL—GROUPS II AND III
Determinate cases

Age	Died	Alive	Total	Rate
20–29	1	4	5	
30–	21	18	39	45%
40–	20	22	42	52%
50–	12	21	33	64%
60–	7	24	31	77%
70–	1	1	2	
80	1	1	2	
Group II and III total	63	91	154	59%
Group I	1	24	25	96%
Group IV	24	5	29	17%

CANCER OF THE CERVIX AND PREGNANCY

Only 2 cases of carcinoma of the cervix were referred while pregnant. One has survived nine years after radium therapy and total hysterectomy in the fifth month of gestation (no cancer found in the surgical specimen six weeks after radium). The other stopped treatment begun after cesarean section in the eighth month of gestation, returned seven months later with advanced disease, and died after further roentgen therapy. Three other determinate cases probably had cancer at the time of delivery and have died, 2 with bizarre, widespread metastasis.

CANCER OF THE CERVIX AND SYPHILIS

We are convinced that there is a definite correlation between cancer of the cervix and syphilis. In this series we have had to depend upon serologic diagnosis in almost all cases. Relatively few patients gave a history of infection or of previous antiluetic therapy. Such information as we have is too scanty and unreliable to correlate arsenical treatment with cervical cancer. There are very few reports on the incidence of syphilis

in cervical cancer, so this series is reported in detail.

TABLE IX

SYPHILIS ASSOCIATED WITH CANCER
(All cases having serologic tests, 1935–1944)

Total Series	Serology Negative	Serology Positive	Total	Infection Rate	Expected* Infection Rate
228 white	108	19	127	15%	2%
68 Negro	33	15	48	31%	25%

* Syphilitic infection rate for females in Delaware, from the State Board of Health.

No significant variation in the extent of disease could be found in syphilitic cases. There was no apparent difference in the survival rate of syphilitic cases. In the determinate group of 208 cases there were 93 white patients surviving three years; 65 had serologic tests and 9, or 14 per cent, were positive. There were 27 Negro patients surviving three years or more; 24 had serologic tests and 8, or 33 per cent, were positive. These survival rates correspond almost exactly with the incidence of syphilis in the entire series.

RACE

Three significant findings are reported with regard to the relation of cervical cancer to race. First, it appears at an earlier average in Negro women (Table VI). Second, the disease is usually more advanced on admission (Table III). Third, there seems to be no difference in curability in spite of this (Table X). We can only explain this last finding by an impression we have formed: the fortitude and stamina of the Negro patient enable her to survive treatment one would hesitate to use on the white patient. The earlier incidence is probably due to earlier pregnancies, earlier venereal infections, and less medical attention for chronic cervical infections.

SURGICAL INDICATIONS

There are a few cases in which surgical treatment is strongly indicated. In this series there was 1 case treated by surgery alone. This patient had an amputation of the cervix for carcinoma in situ, and has remained well over three years. One patient had a vaginal hysterectomy for third degree prolapse following preliminary contact roentgen therapy of the protruding cervical cancer. One pregnant patient had a total hysterectomy for suspected residual cancer six weeks after moderate radium therapy; the surgical specimen was negative. One patient had posterior colpotomy for a pelvic abscess.

Two patients, both of whom died shortly, had hysterectomy for pyometra in 1935. Since then we have treated all cases of pyometra by repeated office dilatation, intrauterine irrigations, removal of slough, and chemotherapy. A most useful agent in treating such cases is zinc peroxide applied daily as a creamy suspension or by insufflation of the powder. This chemical releases nascent oxygen gradually over a twenty-four hour period, and is very effective in controlling the foul, anaerobic infections always encountered. Pyometra not controllable by such methods is due to residual sloughing cancer, and is rarely amenable to surgical cure.

TABLE X

THREE YEAR SURVIVALS BY RACE
1935–1944

	No.	Per Cent	Alive	Survival Rate
White	164	79	95	57%
Negro	44	21	25	57%
Total	208	100	120	57%

PRINCIPLES OF RADIOTHERAPY

It is neither practical nor wise to set up a standard technique to be rigidly employed in all cases. Age, obesity, complicating diseases and prior hysterectomy must be considered in relation to the extent of the disease. Repeated examination of the patient while under treatment is important,

and is often neglected, both by radiologists and gynecologists. It is now generally agreed that combined roentgen and radium therapy is superior to radium therapy alone. Unfortunately, few gynecologists take responsibility for the patient's roentgen therapy, and few radiologists take much interest in the clinical examination of patients referred to them after previous radium therapy. The great majority of the patients in this series had their entire treatment planned and executed by one individual, who was thus enabled to acquire the experience necessary to give adequate irradiation without too high morbidity or mortality from treatment. We have followed certain general principles of radiotherapy in all cases, varying details to suit the needs of the individual case. The results in this series can be ascribed to strict adherence to these principles, which are described below.

(1) *Roentgen therapy should precede radium therapy in most cases.* Bleeding usually stops within ten days and the patient's blood count improves during treatment. (We have seen moderate leukopenia but never anemia resulting from pelvic irradiation.) Infection and slough decrease. Bulky tumors regress, sometimes completely, facilitating radium therapy. Examinations during treatment give valuable information, whereas examination at the peak of intense local reaction to prior radium therapy is seldom satisfactory. Subsequent radium therapy, with its inevitable trauma, is given to a partially devitalized cancer, less likely to be disseminated by the necessary manipulations, to a smaller, easily visible, less bloody, less infected lesion. Exceptions to this general rule occur, notably the early cancer, the endocervical cancer first found at curettage, and the patient who cannot or will not benefit by roentgen therapy (the very obese, crippled, debilitated or mentally infirm).

Gynecologists sometimes fear that patients will not return for radium therapy if roentgen therapy is administered first. This will not occur if they personally supervise the treatment, at least to the extent of seeing the patient weekly. Of 208 cases, we have had only 2 probably curable patients stop treatment.

(2) *Whenever possible treatment should be continuous.* The condition of the patient, such as radiation sickness, severe erythema or extensive slough, may make one or more rest periods imperative, but in general it is planned to give all treatment within six to eight weeks. An interval of more than four weeks between roentgen and radium therapy probably allows the cancer to recover somewhat from the first course of treatment. (Some of the worst recurrent cases we have seen are those given intermittent moderate irradiation until eventual overdosage occurs.)

(3) *The initial treatment plan should be to give the maximum dose tolerated rather than the minimum curative dose.* Some irradiation injuries will occur and are undesirable; they cannot be eliminated entirely without reducing the survival rate. Minor injuries, such as proctitis, pyometra, cystitis and blistering of the skin, are of no importance in the treatment of so lethal a disease. Severe injuries and even death from treatment, if rare, are justifiable. If radical radiation therapy is to be on a par with radical surgery, it must accept similar risks.

(4) *Unnecessary treatment to normal tissues should be avoided* when consistent with the principle just described. The bladder and rectum are protected by displacing them with packing during radium therapy, and by using a retention catheter to keep the bladder empty and away from the radium-bearing uterus. Radium dosage is decreased when a contracted vaginal apex prevents such displacement, and also in cancer of the cervical stump. In the latter, the bladder covers the upper end of the stump since the bladder reflection of the peritoneum was sutured to the posterior vaginal wall at operation, and intestinal loops may be adherent in the cul-de-sac. Perforation of the uterus during dilatation occasionally occurs and contraindicates radium insertion, which is sometimes possi-

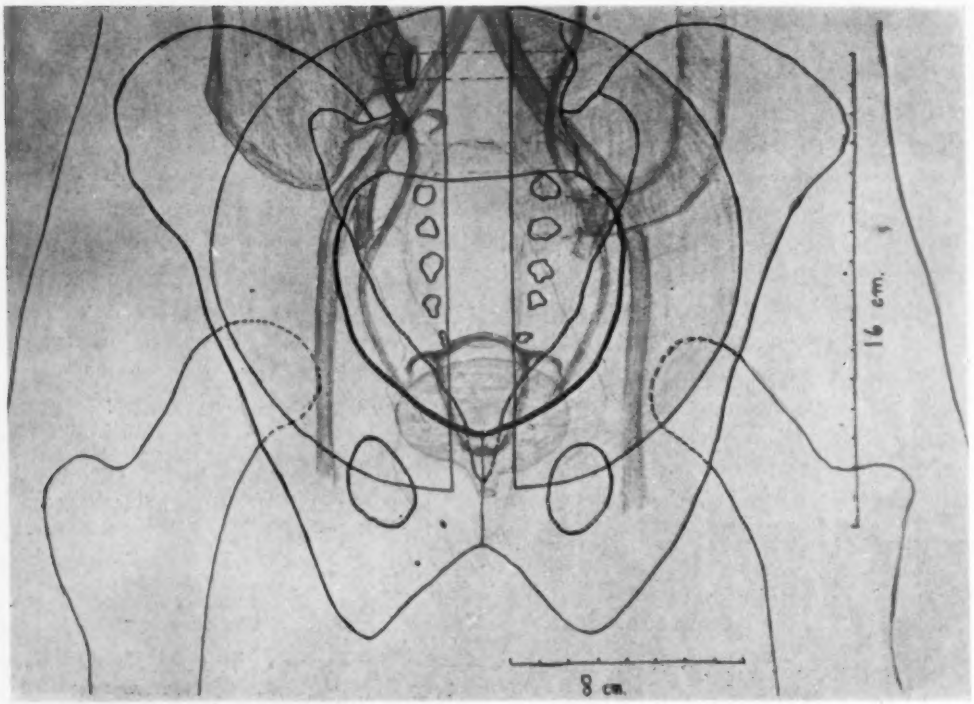

FIG. 1. Anatomic sketch showing relations of 16 by 8 cm. semicircular fields to underlying structures in an average pelvis.

ble at a later date. Perforation of the uterus has never required laparotomy in our experience.

(5) *Roentgen treatment should be limited to the areas of known and probable disease.* By separating the fields in the midline and *not* angulating the beam, the bladder and rectum are spared somewhat and the dose to the parametrium and iliac nodes is not decreased. Large fields should be avoided; they increase the depth dose by backscatter, at the expense of increased damage to normal tissue. We confine treatment to semicircular fields on each side from umbilicus to mid-symphysis anteriorly, from iliac crest to coccyx posteriorly (Fig. 1 and 2). Anatomically, these fields include in the direct beam the parametrium, true pelvis and iliac vessels to the aortic bifurcation. There is no upper, outer corner to irradiate the cecum and the descending colon unnecessarily. They do not include the groin and femoral neck below. The average patient requires a semicircle of 16 cm. diameter (16 by 8 cm.). Occasionally larger or smaller circles are employed. This type of field was evolved from discussions held in 1935 with Hayes Martin[4] and has been used since then.

Reduction of the area of the treatment field to approximately 100 sq. cm. as described above, permits higher dosage in the direct beam, partly because of less skin damage, but particularly because of the decreased damage to deeper structures, and decreased systemic effect, since the volume of tissue irradiated is proportional to the size of the field. The average patient receives from 2,400 to 3,000 roentgens, as measured in air, through each of the four fields described. Lateral fields were discontinued in 1935 on the basis that the added dose to the parametrium was not enough to justify the increased volume irradiated; we deliver a larger dose to the mid-pelvis with greater economy of the patient's physical resources by increasing the anterior and posterior dose. We have had no single instance of pathologic fracture of the femoral neck in this series.

(6) *The whole patient requires treatment during and after therapy.* It is unnecessary to describe the treatment of anemia, infection, cystitis or proctitis. The use of zinc peroxide for anaerobic infections was described above. Radiation sickness rarely proves troublesome; when it occurs amphetamine or desoxy-ephedrine have been the most effective remedies. Severe post-irradiation colitis (rather than proctitis) sometimes taxes our ingenuity. Dietary management, bismuth, opium, belladonna and allied drugs, metamucil, and starch enemas have all been used, with varying success. Surgical treatment has been necessary in a few cases (see below).

TECHNIQUE

The technique of treatment we have employed most frequently consists of preliminary roentgen therapy (200 kv., peak, filtration 0.5 mm. Cu, half-value layer 0.9 mm. Cu), followed by intrauterine radium therapy within ten days.

Roentgen therapy is given five or six days weekly, alternating anterior and posterior pelvic treatment fields, at the rate of 200 roentgens (measured in air) through each of two fields daily. The usual target-skin distance is 70 cm.; for patients whose sagittal diameter is greater than 20 cm., this is increased to 100 cm. to obtain a larger depth dose. Each skin field is a semicircle measuring 16 by 8 cm. in size (100 sq. cm.); size may be varied from 14 by 7 cm. to 20 by 10 cm., depending on the size of the patient. Obese patients, in whom accurate identification of landmarks is more

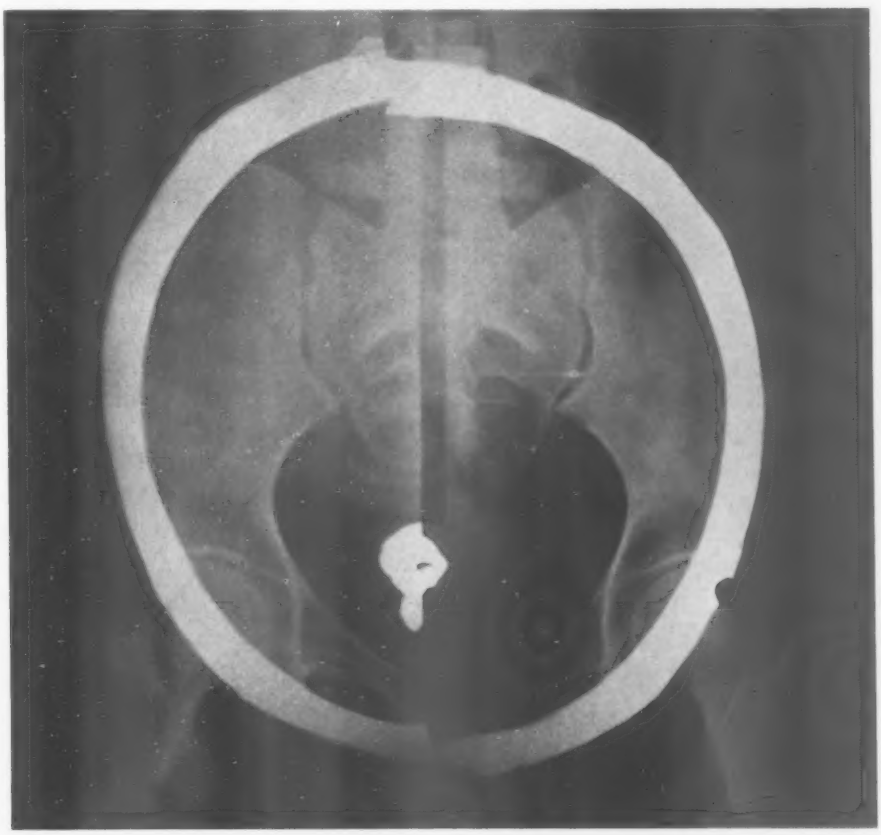

Fig. 2. Double exposure roentgenogram with each side of pelvis exposed separately. The beam is centered over the treatment field, hence about 10 cm. from the midline. A plastic lead plug marks the vaginal apex. The target-skin distance is 70 cm.; the fields 16 by 8 cm. are separated 3 cm. in the midline, but the beams overlap at the level of the cervix.

difficult, require larger fields. The fields are separated 2 to 3 cm. in the midline, and the beam is directed perpendicular to the center of each field, since our target is the parametrium and the regional nodes rather than the cervix. Angulation of the beam is avoided, since we wish to spare the bladder and rectum excessive treatment. Very little cross firing results, as shown roentgenographically in Figure 2. Our best results have been in those patients receiving a total dose of 2,400 r to 3,000 r through each of the four fields described in four to six weeks (Table XI).

Pervaginal (transvaginal) roentgen therapy was given to 37 patients. In these cases, external irradiation and/or radium therapy is decreased slightly. We use treatment cones from 3.5 to 5 cm. internal diameter and give 400 to 500 roentgens of unfiltered 140 kv. roentgen rays per treatment. After inserting the cone and engaging the cervix in its open end (horizontal beam, patient in lithotomy position), the beam is angulated laterally toward the parametrium and pelvic wall by rotating the treatment table and patient about the cone as an axis. We have given doses as high as 2,000 r (4 × 500 r) through each vaginal fornix.

We have been unable to draw conclusions as to the effectiveness of pervaginal roentgen therapy. The slightly poorer results (Table XI) are probably due to its use in more advanced cases. At present we use pervaginal therapy in some cases to supplement radium therapy, but do not employ it routinely. This approach is only practical in patients with a flexible introitus which admits a treatment cone of 4 to 5 cm. internal diameter. The dose to the cervix and broad ligament is increased, but both are within the range of effective radium therapy. It is very difficult to determine the exact direction of the beam beyond the base of the broad ligament; hence the graver problem of controlling nodal metastasis is not solved by pervaginal roentgen therapy.

Radium is applied by placing a 2:1 tandem, 5 cm. in length, in the uterine canal. This contains 75 mg. of radium with 1.0 mm. of platinum filtration, so arranged that 50 mg. lies in the cervical canal and 25 mg. in the lower half of the corpus. It may be left in place for sixty to eighty hours, giving a dose of 4,500 to 6,000 milligram-hours. Occasionally a longer applicator to include also the uterine fundus is used, and the dose increased about 20 per cent. If the vaginal fornices are well preserved, a two-cell colpostat may be used, and the radium dose increased. We seldom give more than 4,500 mg-hr. with the tandem described above; doses of 6,000 mg-hr. should usually be distributed over a larger volume of tissue, as when the colpostat can be used. We have used parametrial needles only twice. On each occasion the patient had carcinoma of the cervical stump, with a palpable parametrial mass in which to insert the needles, and too short a canal and too contracted a vaginal apex to make adequate radium therapy otherwise possible. These 2 patients survive nine and eight years respectively.

Our best results have been obtained with radium doses of from 4,500 to 6,000 mg-hr. given in combination with the roentgen therapy previously described. A few very young patients have tolerated heavier dosage (up to 9,000 mg-hr.), but we believe

TABLE XI

RESULTS OF VARIOUS THERAPY TECHNIQUES

Roentgen Therapy		Radium Therapy (milligram-hours)	Five Year Survival	Rate
External	Pervaginal			
4 × 2400 −3000 r	—	4500–6000	39/59	66%
4 × 2000 −2400 r	Yes	4500–6000	21/37	57%
4 × 3000	—	3600	12/24	50%
4 × 1500 −2000 r	—	6000–9000	3/3	
—	—	3600–6000	1/4	25%
4 × 3000 −4000 r	—	None	0/22	0

such doses would be disastrous for most patients. We never attempt to give further treatment to patients who have had combined treatment such as described. We are convinced that continuous treatment gives the best results. The common practice of allowing several months to elapse between radium and roentgen therapy is to be condemned. Roentgen therapy given three months or more (and perhaps less) after radium therapy is valueless if the patient has residual disease and equally valueless if her cancer has been cured by radium.

IRRADIATION INJURIES

Deaths. Four deaths resulted directly from irradiation and 1 indirectly, only 1 of which has occurred since 1935. One patient, not seen by the author, apparently had perforation of the uterus at the first attempt to insert radium. A week or two later radium therapy (3,000 mg-hr.) was given. Twenty days later she had a free perforation of the rectum and died shortly. From the record one may conclude that her death was due to a technical error; that the radium penetrated the uterine wall to lie in contact with the rectum, causing focal necrosis. One patient developed pelvic peritonitis three weeks after radium therapy, probably from an unrecognized tuboovarian abscess that was stirred into activity. One very thin patient suffered severe radiation sickness and died one month after treatment was completed. We believe the dose to her intestinal tract was excessive and that enterocolitis was the cause of death. In 1941 another extremely thin patient developed obstructive symptoms three months after treatment, had a gangrenous terminal ileum removed surgically, and later died from infection and necrosis of the abdominal wall. One patient in 1935 had total hysterectomy for postirradiation pyometra and died from ascending urinary tract infection, an indirect result of irradiation.

Colitis. Many patients had mild to moderate colitis during treatment which subsided without sequelae. (Several patients with recurring bouts of colitis since treatment show roentgenographic evidence of generalized colitis and/or diverticulosis not confined to the pelvic colon, and are not considered irradiation injuries.) Six patients had severe late irradiation colitis with partial to complete obstruction, two of whom required colostomy for relief, the others* subsiding under careful medical management in the hospital. In 1 case, obstruction due to edema and ulceration subsided, permitting closure of the colostomy; the other has a permanent stricture and will require resection. These cases and the death following resection of the ileum have been reported by Spackman.[11] Two patients with pelvic abscesses (1 diverticulitis, 1 tuboovarian) had vaginal drainage with temporary rectovaginal fistulae which closed spontaneously. The role of radiotherapy is doubtful in these cases.

Ulceration of Bladder. Only 2 cases of late irradiation ulcer uncomplicated by recurrent disease were found.

Fistulae. There have been 3 cases of vesicovaginal fistula not due to recurrent disease. One patient, treated in 1935, had the fistula repaired in 1936 and died of heart disease in 1946. A second patient, treated in 1935, had a fistula of long standing at her first return visit in 1946; repair failed. A third patient, treated in 1942 for Group IV cancer of two years' duration, is alive but has refused surgical treatment. (She had received very heavy pervaginal irradiation in addition to a full dose of external radiation and radium in an attempt to control a hopelessly advanced cancer.) Three other vesicovaginal fistulae, and 1 rectovaginal fistula are reported to have occurred from extension of cancer.

Pyometra. As stated previously, this complication is only serious when due to persistent sloughing cancer. It occurred in 35 of 208 cases, 7 of whom died subsequently (none from pyometra, unless we so classify 2 cases in 1935 whose death may have been

* One of these patients, since this article was submitted for publication, has had resection of the colon for stricture eight years after treatment.

hastened by hysterectomy). Since 80 per cent of those with pyometra are among the three year survivors, it might almost be taken as a favorable prognostic sign!

Skin. It is estimated that 1 patient in 20 has marked atrophy and telangectasia from the doses of roentgen rays described (2,400 to 3,000 r per field in four to six weeks). No accurate figures are available. One patient has definite keratotic changes which may require surgical treatment. One patient had postoperative infection and necrosis of the abdominal wall after resection of the ileum as described above.

TABLE XII

SURVIVAL BY YEAR OF TREATMENT

Year	Admitted	Determinate	Five Year Survival
1935	27	17	5
1936	17	10	4
1937	23	15	10
1938	31	22	11
1939	43	34	20
1940	20	14	5
1941	32	25	15
1942	28	19	10
1943	32	21	13*
1944	43	31	17*

* Three year survival.

Bone. No fractures of the femur have occurred in the determinate group. Several pathologic fractures of the pubis have occurred from metastatic carcinoma.

RESULTS OF TREATMENT

From the determinate group of 156 cases treated from 1935 to 1942 there are 80 cases surviving five or more years, or 51 per cent. In the entire series of 208 cases from 1935 to 1944, 120 cases survived three or more years, or 57 per cent. Others have shown that 10 to 15 per cent of treated patients die from recurrent disease between the third and fifth years, which corresponds to the results in this series (Table 11).

A summary of the results by years shows a definite improvement in 1935, and little change thereafter (Table XII).

RECURRENT CANCER AFTER FIVE YEAR SURVIVAL

It may be of interest to report the cause of death in cases who survived longer than five years. There were 19 survivors of 42 determinate cases from 1935 to 1937 who might now be living ten or more years. One was lost to follow-up; 1 died from general paresis, and 1 from hypertensive cardiovascular disease in the sixth year. One died from metastatic cancer (iliac nodes, ilium) in the eighth year. Fifteen survived ten years. Since then 1 has died in the twelfth year from hypertensive cardiovascular disease and 1 in the eleventh year from a myosarcoma of the uterus which developed during the ninth year after treatment.

Of the remaining survivors (51 from six to nine years), 1 has died in the eighth year and 2 in the sixth year from recurrent cancer, 1 has been lost, and the rest are known to be alive. In all, we have now seen 4 recurrences among 93 patients surviving from six to twelve years, 1 uterine myosarcoma, 3 deaths from intercurrent disease, and have lost 2 patients. The recurrence rate after five years is therefore less than 5 per cent.

COMPARATIVE RESULTS

It is difficult to compare the results reported by various authors. Inevitably some selection of cases must take place. The absolute cure rate is of value in estimating cancer cures in a given region or population, but cannot compensate for all factors affecting the selection of a limited series. For example, the character of the institution making the report affects selection: a home for incurables admits advanced or recurrent cancers; an established cancer clinic attracts cases in whom previous treatment has failed, and cases for consultation who are under treatment elsewhere. One clinic may refuse admission except to ambulatory patients. Another may not record the primary cancer if it is healed, but only the condition existing on admission. This series is selected to show the results of a particular method of treatment, hence untreated

cases and cases recurrent after inadequate treatment elsewhere have not been analyzed. For the convenience of the reader, all cases are summarized in Table XIII.

TABLE XIII

FIVE YEAR SURVIVAL, CANCER OF CERVIX, BASED ON COMPLETE AND SELECTED TOTALS (1935–1942)

Based on determine group described above	156	80
Plus, 1 case lost while well 3 years	157	80
Plus, 5 cases dying of known intercurrent disease	162	80
Plus, 17 cases with recurrent cancer of the cervix, treated for palliation	179	83
Plus, 6 cases with healed cervix, treated for metastasis	185	83
Plus, 13 cases too ill or to distant to report (untreated)	198	83[a]
Plus, 8 cases of recurrent cancer complicated by radionecrosis (untreated)	206	83[a]
Plus 5 cases treated elsewhere and examined by us	211	85[b]
Plus, 10 cases refusing treatment, probably going elsewhere	221	85[c]

[a] Plus possible survivors treated elsewhere.
[b] Two survivors were not treated by us.
[c] See [a]. No attempt was made to trace cases treated elsewhere.

Comparison with surgical results is even more difficult because of the further selection involved in determining operability. For discussion, we may assume that all Group I and II cancers are operable, that Group III cancers might be accepted by some surgeons and rejected by others, and that all Group IV cancers are inoperable. This assumption makes no allowances for the rejection of surgical patients for age, obesity, and complicating disease, factors which are no bar to radiation therapy.

One of the largest surgical series is that of Bonney,[2] who had 40 per cent five year survivors from 500 surgical cases; 52 per cent of 300 cases free of metastatic nodes and 22 per cent of 200 cases with metastatic nodes. In our series of 156 cases, 133 might have been considered technically operable (Groups I to III) and 78, or 58 per cent, survive. If only the 76 Group I and II cases are considered, 71 per cent survive five years. There are 75 per cent three year survivors (80/106) in Groups I and II, unselected for age or physical condition. These "operable" cases comprise 50 per cent of our series and with the Group III "borderline" cases, 85 per cent, while Bonney's operability is estimated to have been about 60 per cent, and Meigs'[6] about 15 per cent. A similar comparison has recently been made by Arneson,[1] using the reports of Pitts and Waterman. Meigs has stated that surgical removal protects the patient against recurrence *in the cervix*. Our three and five year survival rates in "operable" (Group I and II) cases indicate a 5 per cent rate for *all* recurrences during the fourth and fifth years.

The foregoing discussion leads to two conclusions. First, that no final answer can be given as to the best method of treatment of cervical cancer, for lack of comparative data. As yet no properly controlled series comparing surgical and radiotherapeutic methods has been reported. Such a series no

TABLE XIV

RADIATION RESULTS IN OPERABLE CASES (FROM TABLE II)

	1935–42 (5 years)			1935–44 (3 years)		
Group	Per Cent of Series	Survival	Rate	Per Cent of Series	Survival	Rate
I	10%	14/16	87%	12%	24/25	96%
I and II	50%	54/76	71%	50%	80/106	75%
I, II, III	85%	78/133	58%	86%	115/179	64%
All	100%	80/156	51%	100%	120/208	57%

doubt is under way, but may be subject to the criticism that it represents the work of a group of varying competence, rather than that of an individual. Second, the recrudescence of radical surgical treatment may prove harmful to the majority of patients, since in spite of warnings in the surgical literature, incompetent surgeons feel encouraged to attempt "modified Wertheim" operations.

The problem of reaching a decision as to the proper scope of surgical and radiotherapeutic methods is not one to be solved by debate between the proponents of each method. It is a problem to which everyone interested in the treatment of cervical cancer should seek the answer. It is suggested that the American Radium Society could help solve the problem by supporting a controlled study somewhat as follows: One or several institutions with an adequate supply of clinical material would have to cooperate. Cases for comparison should be selected by careful standards. One individual, the surgeon, should select the "operable" cases. Alternate cases, from this group alone, should be treated surgically; if inoperable, they count as surgical failures, even though subsequently irradiated successfully. The alternate cases assigned to radiotherapy should also be treated by one individual. Both gynecologic surgeon and gynecologic radiologist should be chosen on the basis of his previous experience with the method assigned to him.

Until such a series can be studied, surgeons and radiotherapists will point to differences in classification, selection of cases, technical skill, complicating diseases, and many other factors to explain divergent results, and will never fully accept each other's statements. This report is presented to show the results obtainable by radiation therapy of cancer of the cervix uteri in a consecutive series of previously untreated cases. It is believed that the survival rate is equal to or higher than any reported surgical series, and that radiation therapy is suitable for a larger proportion of patients.

SUMMARY

From a total series of 296 cases registered in the tumor clinic of a general hospital, 208 determinate cases of cancer of the cervix uteri have been analyzed. All previously untreated cases who received treatment in this clinic are included, except eight cases dying of unrelated intercurrent disease and one case lost to follow up when free of disease for more than three years. The relation of survival to stage of disease (Schmitz classification), age, race, and duration of symptoms, is tabulated. A relatively high incidence of associated syphilis is reported. Specific indications for surgical treatment are noted. The non-surgical treatment of pyometra is recommended. The general principles of radiation therapy followed are presented, and the technique used is described. Irradiation injuries and deaths (2 per cent) are reported. A three year survival rate of 57 per cent of all cases and 75 per cent of "operable" cases, and a five year survival of 51 per cent of all cases, 71 per cent of "operable" cases, is reported. Deaths after five years are recorded. A plan for controlled comparative study of surgical and radiation treatment is proposed. A plea is made for more careful and more radical radiation therapy.

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RADON TREATMENT OF CANCER OF THE CERVIX UTERI*

A DETAILED REPORT OF 137 CASES

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IN THE fifteen year period between 1929 and 1944, 137 patients suffering with carcinoma of the cervix uteri have been admitted to the Simpson Radium Institute for treatment. This paper deals with a study of these cases.

In our practice we rely altogether upon radon as our source of radiation. The treatment is carried out in three stages. We attack the primary tumor mass first with a powerful intravaginal applicator placed against the exterior of the cervix. When the tumor mass is so shrunk that it no longer occludes the cervical canal one intrauterine application is given. As a final measure the "pelvic girdle" is irradiated from the skin surface with the radon bomb.

INTRAVAGINAL TREATMENT

It is most important to avoid traumatism, to reduce infection and to stop bleeding. As in malignant tumors elsewhere, the spreading edges of the cancer should be irradiated first. We begin treatment by irradiating the exterior of the cervix. The end of the cervix and the lateral fornices of the vagina are used as treatment areas. The radon applicator is a flat, silver box loaded with several radon tubes laid side by side. The applicator is covered with from 4 to 10 mm. of rubber and a sterile fingercot.

With the patient in the lithotomy position the cervix is gently exposed with a long bivalve speculum. A gold plate 4 mm. thick and large enough to cover the distal third of the inner surface of the posterior blade of the speculum is inserted to help shield the rectum from the rays.

The radon applicator is grasped with an 8 inch rat-toothed forceps and placed anterior to the gold plate either against the end of the cervix or in one of the lateral fornices. A small amount of gauze is gently inserted to push away the lateral vaginal walls and to help keep the applicator in place. The speculum, gold plate and forceps carrying the applicator are left in the vagina during each treatment, being held in place by a double T-binder dependent from the patient's shoulders. The treatments last from twenty to thirty minutes each and are given daily, on alternate days or less often, until from 3,000 to 6,000 millicurie-hours has been given. This course of treatment usually lasts about four weeks.

As a result of these cervical applications the infection, discharge and bleeding are arrested; the visible tumor entirely disappears or is markedly reduced in size; the external os, if obscured by the tumor mass, again becomes visible and the cervical canal, if obstructed, again becomes patent. The intrauterine applicator can then be inserted without traumatism or dilation of the cervix.

DOSAGE

In malignant tumors, the "toleration dose" is usually given, i.e., the dose the surrounding normal tissues will safely bear. As malignant tumors have different degrees of radiosensitivity, there is unfortunately no fixed cancer dose. It is to be noted that a series of seances, spread over days or weeks, causes greater effects on cancer cells and relatively smaller effects on normal cells than the same dose given in a single seance. One should not try, therefore, to cause resolution of the cancer by a *single seance;* better results are to be had if a *series of seances are given.*

With an intravaginal applicator measureing laterally 2.5 by 2.5 cm. screened with 2

* Presented at the Twenty-ninth Annual Meeting, American Radium Society, Atlantic City, N. J., June 9–10, 1947.

mm. of silver and 1 cm. of soft rubber, the single erythema skin dose (e.s.d.) is approximately 290 mc-hr.

If the irradiation is given in two, three, four, or seven equal seances, the dose may be increased 30 per cent (i.e., to 377 mc-hr.); 50 per cent (i.e., to 435 mc-hr.); 60 per cent (i.e., to 464 mc-hr.); and 110 per cent (i.e., to 609 mc-hr.), respectively.

One may give as a rule, about 2.5 e.s.d., i.e., 1,522 mc-hr. (2.5×609) in seven seances to each of the three portals used, i.e. to the end of the cervix and the two lateral fornices.

In the course of a few weeks, a total dose of about 4,566 mc-hr. (3×1,522) may be given intravaginally to the exterior surface of the cancerous cervix, provided there is no overlapping of the irradiations at the surface of the original mucous membrane.

INTRAUTERINE TREATMENT

After the treatment of the exterior of the cervix has been completed the intrauterine treatment is given. As the tumor often extends above the internal os the applicator should extend to the fundus of the uterus.

The intrauterine applicator is a lead tube which can be easily bent to the uterine curve. It has an external diameter of 4 mm. and a wall thickness of 1 mm. These tubes are made in different lengths so as to hold from two to five radon tubes in tandem.

With the patient in the lithotomy position the cervix is exposed with a speculum and the length and curve of the uterus are measured with a uterine sound. An intrauterine applicator of the proper length is loaded and bent to the shape of the uterus. This is gently inserted without dilation, "pulling down," or otherwise traumatizing the cervix. A vaginal pack holds the applicator in place. As a rule only one treatment lasting from two to four hours is given. The dosage is approximately 1,800 mc-hr. with an applicator 7 cm. in length.

TRANSCUTANEOUS IRRADIATION

After treatment of the cervix and the interior of the uterus has been completed external irradiation is given at a distance of 4 to 6 cm. from the surface of the skin. The radon applicator is a flat silver box in which a number of radon tubules, containing from 500 to 1,000 mc. or more of radon, are laid side by side. Four portals are used, two anterior and two posterior. With the patient lying on a table, a balsa wood block 6 cm. square and of the desired thickness is strapped to the patient's skin. A lead guard is lowered around the block. The radon applicator is placed inside the guard and rests upon the balsa wood block.

DIVIDED DOSE TECHNIQUE

The divided dose technique is used for the following reasons:

1. There is no fixed "cancer dose." Each tumor must be treated until it yields or until the "toleration dose" has been given.
2. Tumor cells are known to be most sensitive during mitosis and not all cells of a given tumor are in the process of division at the same time.
3. The exact dose tolerated by any one patient cannot be known in advance. To insure destruction of the growth, the greatest dose should be used that can be given with safety.
4. A much greater total dosage can be given if the treatment is administered in several seances.
5. Giving internal treatments of short duration to the exterior of the cervix precludes the danger of damming up uterine discharge with resulting pelvic infection.

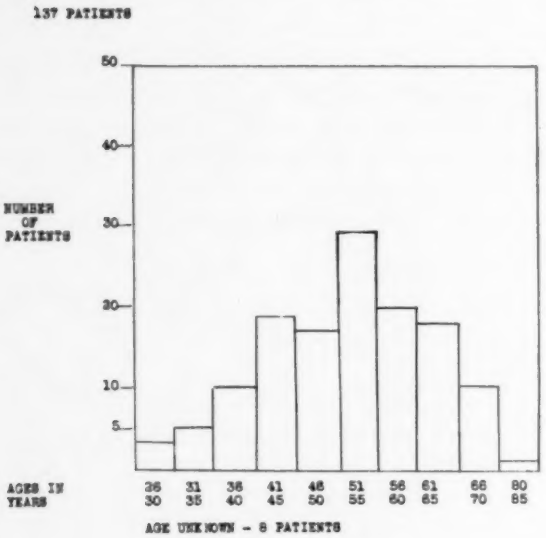
MATERIAL

The patients in our group compare in age, marital status and duration of symptoms with those reported by Healy and Twombly, and many others. The ages vary from twenty-six to eighty-five with 29 patients, or 21 per cent, in the fifty-one to fifty-five year group (Graph 1).

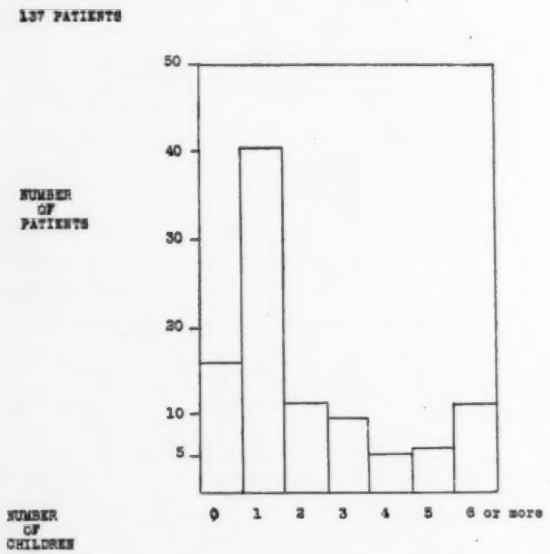
One hundred twenty-nine, or 94 per cent, of our cases were or had been married. Seven had never married and the status of 1 is unknown. Eighty-nine per cent of our patients had borne children, with the majority (74 per cent) bearing several (Graph 11).

The duration of symptoms varied from two weeks to three years. Forty-nine per cent waited six months or longer before seeking medical aid (Graph III).

The biopsies of some of our patients were



GRAPH I. Ages of patients.

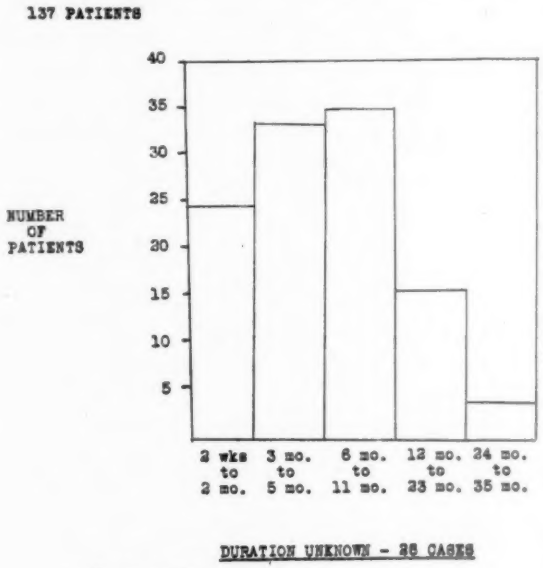


GRAPH II. Number of children borne by patients.

taken by the referring physician and diagnosed by the pathologist in the local hospital. Many of these pathologists made no effort to grade the tumor in accordance with Broders' classification. Of these cases graded, 4 per cent were in Grade 1, 69 per cent in Grade 2, 25 per cent in Grade 3 and 2 per cent in Grade 4. In our series were 131 cases of squamous cell carcinoma, 5 cases of adenocarcinoma and 1 case of myosarcoma.

Of our 137 cases, 13 did not complete treatment. Our detailed report is based upon the remaining 124 cases. One of the discarded cases was the patient suffering with myosarcoma of the cervix. This tumor grew rapidly under intense irradiation and was referred back to the surgeon. A panhysterectomy was done. The patient is alive and well now more than three years after operation.

Our classification of cases into stages is



GRAPH III. Duration of symptoms.

based upon the old League of Nations Classification. It was impossible for us to reclassify our old cases at this late date, with any degree of accuracy. Table 1 presents the detailed information on our cases.

Seven cases were in Stage I, 42 in Stage II, 37 in Stage III and 35 in Stage IV. The stage of 3 cases is unknown.

Of the 124 cases, 4 died under three years without cancer, 63 died under three years with cancer, 54 lived three years or over without cancer and 3 are living over three years with cancer. Forty-five cases lived over five years without cancer.

Of the 7 cases in Stage I, all recovered except 1 who died under three years without cancer.

TABLE I

RESULTS OF TREATMENT, 1929–1944, ACCORDING TO LEAGUE OF NATIONS CLASSIFICATION (OLD)

	Total		Stage I		Stage II		Stage III		Stage IV		Stage Unknown	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
TOTAL	124	100	7	5.6	42	34	37	30	35	28.3	3	2.1
Dead under 3 yr. without cancer	4	3	1	14.3	2	5	1	2.7				
Dead under 3 yr. with cancer	63	51			8	19	21	56.8	32	91.4	2	66.7
Living 3 yr. without cancer	54	43.6	6	85.7	31	73.8	14	37.8	2	5.7	1	33.3
Living 3 yr. with cancer	3	2.4			1	2.2	1	2.7	1	2.9		
5 year recovery record—106 cases—1929 to 1942												
TOTAL	106	100	6	5.7	34	32.1	30	28.3	33	31.1	3	2.8
Living 5 yr. without cancer	45	42.4	5	83.3	27	79	11	36.6	1	3	1	33.3

TABLE II

RESULTS IN 67 CASES RECEIVING INSUFFICIENT EXTERNAL IRRADIATION, 1929–1944, LEAGUE OF NATIONS CLASSIFICATION (OLD)

	Total		Stage I		Stage II		Stage III		Stage IV	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
TOTAL	67	100	5	7.5	27	40.3	22	32.8	13	19.4
Dead under 3 yr. with cancer	33	49.2			6	22.2	15	68.2	12	92.3
Dead 3 to 5 yr. with cancer	1	1.5							1	7.7
Living 3 to 5 yr. with cancer	1	1.5					1	4.5		
Living 3 yr. without cancer	32	47.8	5	100	21	77.8	6	27.3		
48 cases—(1929 to 1942)—5 year clinical recoveries										
TOTAL	48	100	4	8.3	18	37.5	15	31.3	11	22.9
Living 5 yr. without cancer	22	45.8	4	100	14	77.7	4	26.6	0	0

Of the 42 cases in Stage II, 2 died under three years without cancer, 8 died under three years with cancer, 1 is living over three years with cancer, 31 lived three years or over without cancer and 27 lived five years without cancer.

Of the 37 cases in Stage III, 1 died under three years without cancer, 21 died under three years with cancer. Of those living, 14 have lived three years without cancer, 1 over three years with cancer and 11 over five years without cancer.

Of the 35 cases in Stage IV, 32 died under three years with cancer, 2 have lived three

years or over without cancer, 1 of which has lived over five years, and 1 has lived over three years with cancer.

Of the 3 cases in which the stage is unknown 2 died under three years with cancer and 1 is alive and well over five years without cancer.

It will be noted that the three year percentage of clinical recoveries is 43.6 per cent and the percentage of five year recoveries is 42.4 per cent.

During the period covered by this report we have come to rely more and more upon internal irradiation. It is well known that glandular metastasis from a squamous cell carcinoma is difficult if not impossible to eradicate by irradiation unless the new growth is very radiosensitive. Taylor and Nathanson in speaking of carcinoma in their book "Lymph Node Metastasis" say, "It is commonly considered that the cures resulting from irradiation alone are probably restricted to those cases in which the disease remains a local process or at most has involved only those nodes immediately adjacent to the cervix."

In Table II, we present 67 cases that we believe have been under-irradiated from the skin surface. These cases have had from none to a total of 16,000 mc-hr. at 4 cm. distance. The high three year (47.8 per cent) and five year recovery percentage (45.8 per cent) in the under-irradiated cases present proof of the fact that patients can get well without much external treatment if the internal treatment is sufficient.

If our deductions are correct the injuries produced by heavy external irradiation to the bladder and bowel, as described by many authors, and to the bony system, as described by Slaughter, are unnecessary.

We believe, however, that the advanced cases, particularly those in which glandular metastasis is known to exist, should receive adequate irradiation. The treatment should be undertaken as a palliative measure, however, and not pushed to the point where injury to normal structures is possible. The one exception would be in radiosensitive tumors wherein even glandular metastases may possibly yield.

SUMMARY

1. One hundred and thirty-seven cases of cancer of the cervix uteri treated with radon between the years 1929 and 1944 are reviewed.

2. The ages of these patients varied from twenty-six to eighty-five, with the largest number, or 21 per cent, in the fifty-one to fifty-five group.

3. One hundred and twenty-nine, or 94 per cent, of our cases were or had been married.

4. Eighty-nine per cent of our cases had borne children. Seventy-four per cent had more than one offspring.

5. The details of the treatment are given.

6. Study of those cases given inadequate external irradiation disclose a five year recovery rate of 45.8 per cent.

7. The five year recovery rate of the entire group is 43.7 per cent.

8. The above result would appear to indicate that irradiation from the skin surface is of secondary importance in early cases of cancer of the cervix uteri.

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CARCINOMA OF THE CERVIX UTERI*

AN ANALYSIS OF 790 CASES TREATED OVER FIVE YEARS AGO

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MY ASSOCIATES and I treated 790 patients with carcinoma of the uterine cervix from 1919 to 1940, inclusive. The diagnosis was established by microscopic histopathologic examination in all cases. The degree of cell differentiation was recorded at the time of treatment, or by reviewing the original slides, or (rarely) by referring to the report of the original pathological examination. Figures as to the delay in treatment, after the initial symptoms, were available in all cases.

All patients were treated by irradiation. In the earlier years radium alone was the usual method of treatment. In the later years most patients were treated by both radium and roentgen irradiation. In recent years we have treated the early tumors, with little or no infection, by radium followed by roentgen irradiation and the late and infected tumors by roentgen irradiation followed by radium. For one reason or another, a few of the patients recently treated have received only radium or only roentgen treatment. However, all patients treated are included in the report.

The five year cures are as follows (Table I):

TABLE I

		5 Year Cures
1919–1940	790 cases	24.9%
1936–1940	94 cases	33.8%

Divided into stages (League of Nations) the five year cures are as shown in Table II.

The tumors are classified, according to their gross appearance, as proliferative or destructive. The five year results are somewhat better in the former (Table III).

TABLE II

		5 Year Cures
Stage I	44 cases	63.6%
Stage II	114 cases	39.5%
Stage III	451 cases	23.1%
Stage IV	111 cases	1.8%
"Stump cases"	55 cases	29.1%
Recurrence in vault after panhysterectomy for cancer of the cervix	15 cases	13.3%

TABLE III

		5 Year Cures
Proliferative type	455 cases	27.9%
Destructive type	335 cases	20.9%

The tumors are classified according to cell differentiation. The five year results are as follows (Table IV):

TABLE IV

		5 Year Cures
Well differentiated squamous cell	207 cases	21.3%
Partially differentiated squamous cell	309 cases	26.9%
Poorly differentiated squamous cell	224 cases	25.0%
Adenocarcinoma	50 cases	28.0%

The degree of cell differentiation apparently bears no relation to five year curability. The small difference that exists is in favor of adenocarcinoma. During this period of observation (1919–1940) one sarcoma of the cervix was observed but is not included in the report.

* Presented at the Twenty-Ninth Annual Meeting, American Radium Society, Atlantic City, N. J., June 9–10, 1947.

The oldest patient treated was seventy-eight. The oldest five year cure was seventy-two, at the time of treatment. The youngest patient treated was twenty. The youngest five year cure was twenty-four, at the time of treatment. In 34 patients thirty years of age or younger, 20.9 per cent five year cures were obtained. The disease seems by no means hopeless in these younger women.

The number of pregnancies seems to have but little influence on the percentage of five year cures (Table v).

Table V

		5 Year Cures
Never pregnant	67 cases	21%
Pregnant 5 or more times	267 cases	24.3%

The difference in the percentage of five year cures in apparently similar groups of white and of Negro patients suggested the following analysis.

The percentage of five year cures is much higher in white than in Negro patients (Table vi).

Table VI

		5 Year Cures
White	659 cases	27.5%
Negro	131 cases	12.2%

Apparently delay in treatment does not account for the difference in results in white and Negro patients (Table vii).

Table VII

White	Average delay	9.4 months
Negro	Average delay	9.9 months

The presence of a positive Wassermann reaction seems to be a lesser liability to the Negro than to the white patient. Wassermann reactions were not obtained in all patients in the early years of the series but the following results may have some significance (Table viii).

Table VIII

			5 Year Cures
White	Negative Wassermann	253 cases	34.8%
White	Positive Wassermann	37 cases	24.3%
Negro	Negative Wassermann	59 cases	15.3%
Negro	Positive Wassermann	28 cases	14.3%

Even for patients in the same stage of the disease (except for the few cases in Stage iv) the results are better in white patients than in Negroes (Table ix).

Table IX

	White		Negro	
	5 Year Cures		5 Year Cures	
Stage i–ii	145 cases	47.0%	13 cases	38.5%
Stage iii	377 cases	25.7%	74 cases	9.5%
Stage iv	84 cases	0.0%	27 cases	7.4%
"Stump"	39 cases	35.9%	16 cases	12.5%

Fifteen cases of carcinoma recurring in the vault after panhysterectomy for carcinoma of the cervix uteri are not included in Table ix.

SUMMARY

1. The five year results of irradiation in a series of 790 cases of carcinoma of the cervix uteri are reported.

2. The influence of stage of disease, gross type, cell differentiation, age and number of pregnancies on the five year results is discussed.

3. Even for patients in the same stage of the disease the results are better in white than in Negro patients. The reason for this difference is not apparent. It does not seem to be due to longer delay in treatment or to poorer results in Negroes with a positive Wassermann reaction.

I wish to thank Dr. A. E. Bennett, Dr. W. F. Boukalik and the house officers at City, St. Alexis, St. Luke's and University Hospitals for their aid in treating these patients and for their interest in the follow-up examinations.

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Vol. 60, No. 3

CANCER OF THE CERVIX UTERI

A STUDY OF FIVE TO ELEVEN YEAR END RESULTS*

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IN MULTIPAROUS women the uterine cervix is most favorably situated for crossfire by accurately placed radium elements: The portio vaginalis protrudes moderately into the vaginal vault allowing the operator to place radium cells into each lateral fornix; with sufficient capacity of the vault a third radium source can be packed against the vaginal surface of the cervix; in most instances the cervical canal can be entered and a chain of radium tubes inserted.

With such an arrangement 15,000 gamma roentgens can be delivered into the cervix uteri proper, a sufficient dose to destroy squamous cell carcinoma. Unfortunately, only a small minority of all women who apply to any tumor clinic have the lesion so confined. Lucas[10] and Arneson[1] have shown how the intensity from this intracavity radium drops off rapidly with each additional centimeter of shell about these radium sources in the pelvis. Roentgen therapy has been called upon to augment the tumor dose into those pelvic structures beyond the cervix proper.

The Brooklyn Cancer Institute serves a large metropolitan population composed of many racial backgrounds. Cases are referred by other city and private hospitals, by practicing physicians and more recently by the local cancer committee. Because of this about 40 per cent of all admissions have received some treatment before admission.

Recently a patient, Mrs. R. C. (Case IV), who had eight years previously been treated for carcinoma of the cervix reported back to the Institute. Her chief complaint was upper abdominal and back pain associated with diarrhea (Fig. 1). On examination her pelvis was found to be free of tumor. A deep fixed mass, however, could be palpated in the intercostal angle slightly to the left of the midline. Every effort, including exploratory laparotomy, to more accurately determine the exact nature and origin of this tumor failed. A needle biopsy was reported as carcinoma (autopsy was refused). It was postulated that while the carcinoma of her uterine cervix was eradicated from her pelvic organs, some cells had migrated into her periaortic lymph nodes and after years of quiescence had finally multiplied to form this large retroperitoneal tumor which caused her death. The only other conclusion to be drawn is to admit that this retroperitoneal carcinoma represented a second primary growth, probably arising in the pancreas.

Another patient, Mrs. P. G., survived treatment for carcinoma of the cervix for twelve years. In this interval, however, she developed a second primary lesion in the bladder and finally died of a retroperitoneal liposarcoma.

Partly because of the interest aroused by these cases it was decided to review all cases of carcinoma of the cervix admitted to the Brooklyn Cancer Institute from 1936 through 1941, services of Dr. Samuel Wolfe and Dr. Joseph McGoldrick. All admissions with diagnosis of carcinoma of the cervix uteri were traced to death or if living into 1947, an interval of from five to eleven years. The staff of the Social Service Department should be given high credit for the relatively few individuals lost to this follow-up. In these six years a total of 230 women were admitted with the diagnosis of cervical carcinoma confirmed by biopsy. Ten additional cases had to be discarded for lack of proof.

Table 1 lists the end results of all cases reviewed.

Eight women in this group have died, having survived over five years after their original treatment. A short summary of these 8 cases follows:

CASE I. M. G., admitted in 1936. After sur-

* Presented at the Twenty-ninth Annual Meeting, American Radium Society, Atlantic City, N. J., June 9–10, 1947.

viving with few symptoms for nine and a half years, this patient died of recurrent pelvic carcinoma. She had developed a left hydronephrosis and hypertension.

Case II. A. R., admitted 1936. Following supracervical hysterectomy this patient was referred for a discovered carcinoma in the stump. She was readmitted in 1941 for a tumor which appeared over her pubis. This was reported as a metastatic lesion most probably from the ovary. She lived over five and a half years after her original admission.

Case III. M. R., admitted in 1937. After five years of comparative good health she became

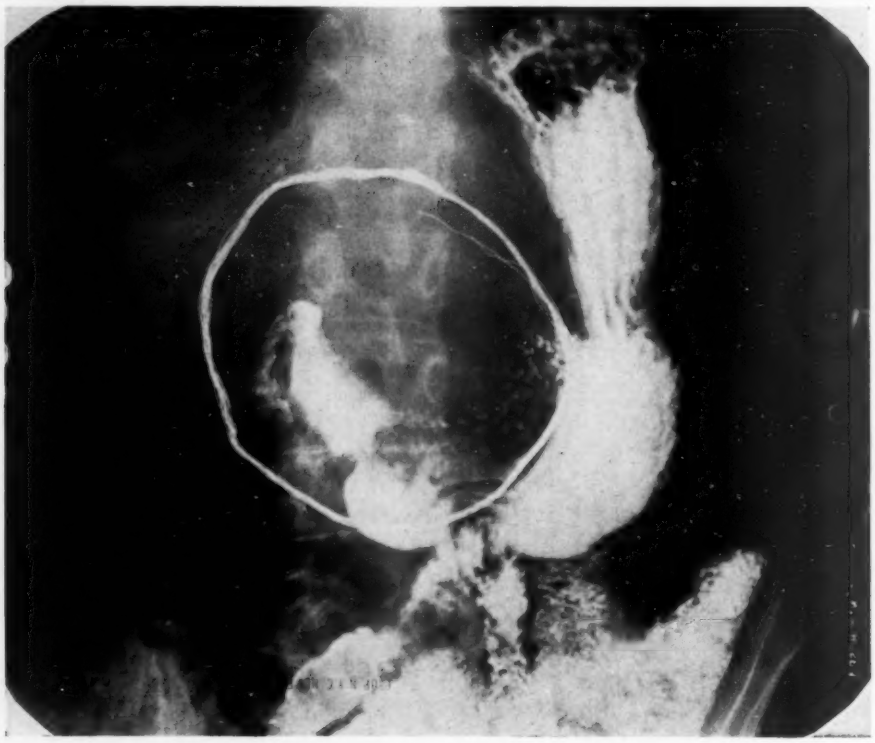


Fig. 1. Mrs. R. C. (Case IV). Eight years previously treated for carcinoma of the cervix. Now admitted with deep fixed mass in upper abdomen as outlined on the roentgenogram. Is this extension of cervical carcinoma or a second primary lesion?

Table I

MORTALITY STATISTICS

Year	Total No.	Lost	Died of Cancer or Factors Due to Cancer	Died of Extraneous Disease	Living
1936	22	2	15	0	5
1937	33	4	26	0	3
1938	47	0	42		5
1939	36	0	24[1]	1[2]	11
1940	52	5	34	1[3]	12
1941	40	4	20	0	16
Total	230	15	161	2	92

[1] May have died from a second primary lesion (pancreas).
[2] Died in diabetic coma, no evidence of pelvic carcinoma.
[3] Died following concussion, no evidence of pelvic carcinoma.

distended with ascites and large peritoneal tumor masses could be felt. Could she not have developed a second primary as ovarian carcinoma?

Case iv. R. C. admitted in 1938. This patient's case history was described above. Eight years after treatment for cervical carcinoma she developed a fixed retroperitoneal carcinoma either a second primary or a latent metastasis to the periaortic lymph nodes.

Case viii. J. P., admitted in 1940. This patient developed intestinal obstruction at the sigmoid flexure. A rectovaginal fistula had also broken through. She survived six and a half years.

MULTIPLE PRIMARY LESIONS

Four cases in this series are known to have developed double primary lesions, 2 in the breast, 1 in the ovary and 1 in the thyroid; another individual developed three primary lesions, breast, rectum and cervix; this besides one individual (1934 series) who in addition to her cervical lesion later developed a bladder carcinoma and still later a retroperitoneal liposarcoma. This is a larger number of multiple primary lesions than would be expected in a similar number of women who might have been placed under study for the same time interval as a control group.

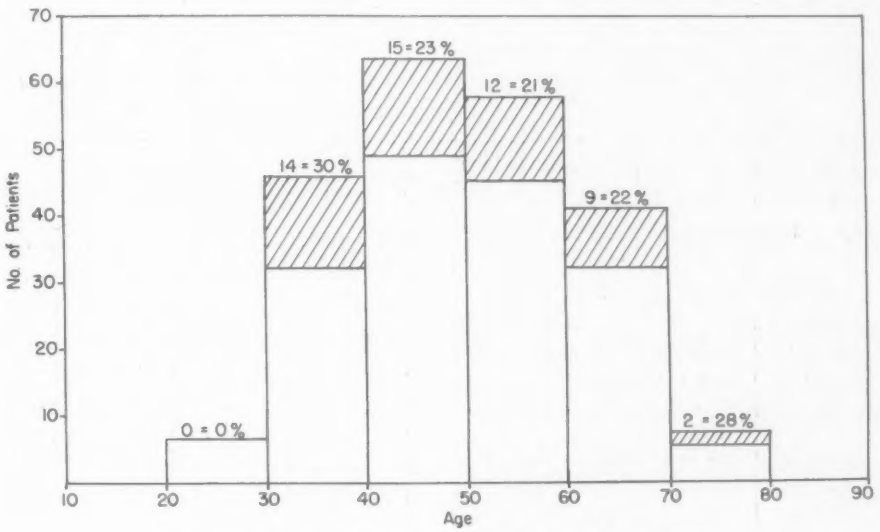


Fig. 2. Age incidence as compared with survival rate.

Case v. M. H., admitted in 1938. A partial intestinal obstruction developed at the level of her sigmoid flexure six years after radiation therapy. There was never any evidence of recurrence of neoplasm in her pelvis.

Case vi. A. G., admitted in 1939. This woman nearly died of an anaphylactic reaction during intravenous injection for urographic study. Because of this reaction she failed to return for follow-up. She was traced by the Social Service Department which found that she had died seven years after admission. Cause of death was not determined.

Case vii. A. G., admitted in 1940. This patient died in diabetic coma over five years after radiation treatment for cervical carcinoma. At her last clinic visit shortly before her death the examiner found no evidence of recurrence or extension of the pelvic tumor.

RACIAL INCIDENCE

Carcinoma of the cervix is known to occur as a rarity among Jewish women. Only 10 women of the Jewish race are listed in this series. This compared with 35 women whose name and religion would indicate that they were of Italian parentage and 35 women of the Negro race.

AGE INCIDENCE

The age incidence closely parallels that of other reported groups. The highest percentage of survivors occurred among those who first reported in their third decade—30 per cent. Not one of those admitted in their twenties survived. This finding is in agreement with the well known fact that cancer, as a rule, becomes disseminated more rapidly in young people (Fig. 2).

NUMBER OF PREGNANCIES

Cervical cancer is more apt to develop in the multiparous woman, in the cervix which has been lacerated through birth injuries. But 4 unmarried women were listed in this series; to these, 7 married women can be added who denied ever having been pregnant. Four others had had but a single pregnancy which ended in miscarriage. All the others had borne at least one child, with one-fourth of all cases having had three or more children. Two women aborted during the early months of pregnancy as a result of carcinoma and irradiation. One of these 2 survives eight years.

PATHOLOGICAL INCIDENCE

From a pathological standpoint, 14 were reported as highly anaplastic growths, the same number as adenocarcinoma. All others were squamous cell carcinoma either of the transitional or more mature prickle cell type. Three of the 14 patients survived with anaplastic carcinoma. Those with the transitional and prickle cell lesions survived in about the same ratio, namely 26 per cent. Those with adenocarcinoma showed a lower survival rate, 14 per cent (Fig. 3).

AUTOPSIES

Although 160 women in this series have died, only 14 autopsies were performed. This low percentage is partially due to the fact that many of these patients were discharged to other institutions or their homes following active therapy at the Cancer Institute.

Eight of the 14 autopsied cases are described as having extensive spread of the carcinoma into the uterine and parametrial tissues. Nine were shown to have advanced hydronephrosis of one or both kidneys, 3 with pyelonephritis and cortical abscesses. Three had metastases to pelvic, mesenteric and peri-aortic lymph glands. Four had distant metastasis to lung, liver and bone (Fig. 4). Two died with a purulent peritonitis most probably associated with intestinal complication. In 4 cases the

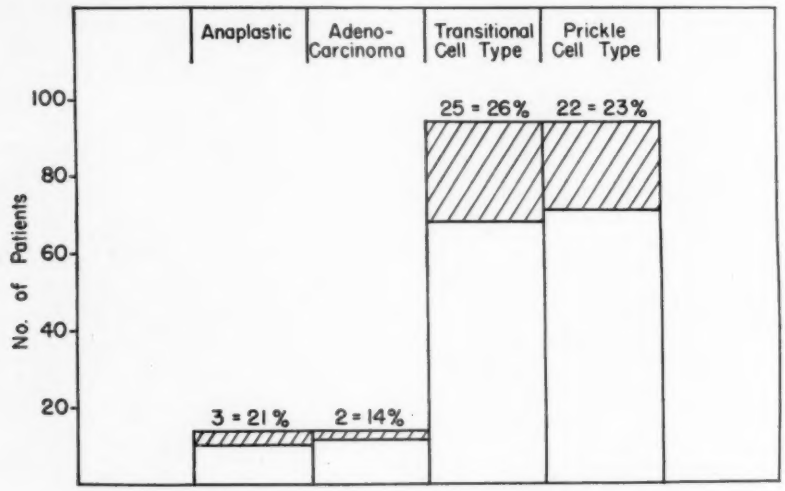


FIG. 3. Pathological type with survival rate.

neoplasm extended into the rectum while in 3 the carcinoma had involved the bladder.

CLASSIFICATION

When first seen all cases were classified in accordance with the classification of Schmitz.[13] For accuracy, any such clinical classification must depend upon the accuity of the examining physician. He may mistake inflammatory masses for cancer, or, on the other hand, he may not appreciate the full extent of the neoplastic process. This latter can be illustrated by a case recently admitted to the hospital where the cervix showed minimal changes simulating cervical erosion. The pathologist, from the small biopsy specimen he had for study, reported intra-epithelial carcinoma. On rectal examination, however, one parametrium was already foreshortened and moderately infiltrated. In view of this evident paracervical extension this case should be classified as Schmitz Group III, though her condition could easily have been mistakenly classified as Schmitz Group I. It is easy to see how errors can be made on both sides of the ledger. Rapid decline in salvage with advancing neoplasm is clearly pictured by this clinical segregation: Schmitz Group I = 61 per cent vs Schmitz Group IV = 8 per cent. The proportionately high salvage in cases of cervical stump is noteworthy, 27 per cent (Fig. 5).

Fig. 4. All metastases to bone were limited to one of the innominate bones and not to the spine or long bones.

BLOCK OF PELVIC LYMPHATICS AND RESULTANT LEG EDEMA

With spread of the carcinoma outward into the parametrial structures the neoplasm not only rings and chokes off the ureter but reaches out and fills the entire pelvis with a cement-like carcinomatous inflammatory mass. Abscess may be locked within this neoplastic process. Such an extension frequently blocks the lymphatics draining the leg and consequently edematous swelling of one leg is an indication of advanced pelvic disease. In many ways this simulates the edema of the arm which oc-

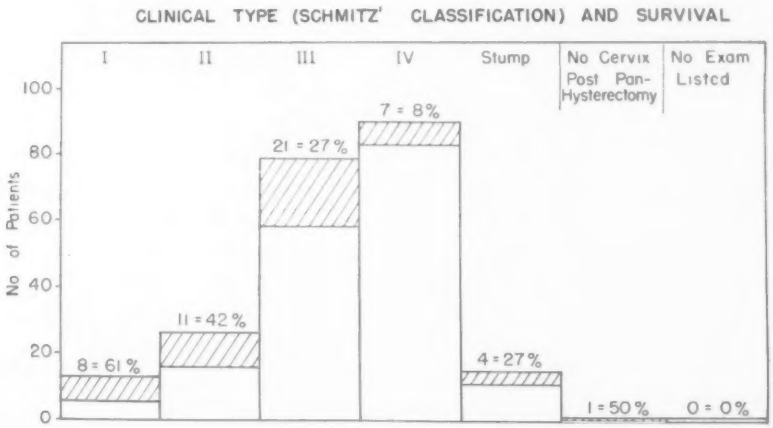


Fig. 5. Clinical type (Schmitz' classification) and survival rate.

curs with advance of carcinoma of the breast into and beyond the axilla. Pressure on the psoas muscle produces flexion deformity of the leg at the hip. This complication does not appear to have received adequate emphasis in the medical literature and in practice its significance is not always understood. In 10 instances in this series edema and flexion deformity of the leg were of sufficient consequence to be recorded as one of the outstanding symptoms.

TREATMENT

Some 40 cases had to have their treatment modified because they received some part of their therapy before entering the Cancer Institute. These do not include those operative procedures which preceded the discovery of the cervical carcinoma by several years. Whenever possible radium and roentgen-ray dosage and operations carried out elsewhere have been compiled along with the irradiation and surgery recorded in the Cancer Institute. Whether treated or not, no proved case was deleted from the list.

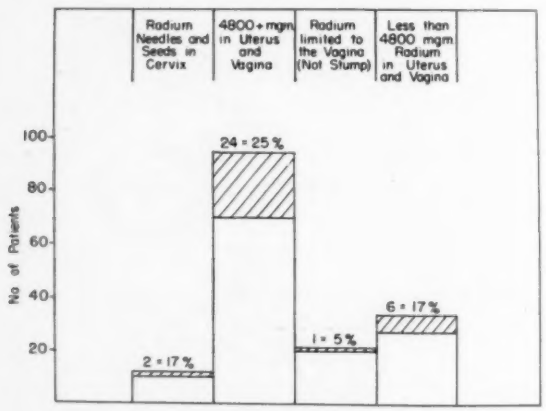


FIG. 6. Modes of radium application with survival rate.

I. *Hysterectomy*. Operative treatment of cervical carcinoma has, on the whole, given place to radiation therapy. There is, however, always that latent desire on the part of the surgeon to eradicate the neoplasm by one operation. Seven patients were hysterectomized (panhysterectomy), one by the vaginal route. Three of these procedures were conducted in other institutions. Three of these women are alive to date. In considering this relatively high survival rate of 43 per cent, it must be remembered that this small group represents a carefully selected few.

II. *Radium*. As a rule, radium is administered after the method used at the Radium Institute of Paris. A three tube tandem of low radium content is inserted into the uterocervical canal; a colpostat is inserted into each lateral fornix with equal units of radium in each arm, and a cork of the same or lesser strength is placed between the arms of this colpostat. At the Cancer Institute this set is not removed daily for cleaning purposes but is left in situ, when tolerated, up to 100 hours. On occasion this arrangement has to be modified:

(a) With a small vagina just two corks can be placed in the vaginal vault.
(b) Very occasionally a vagina will admit but one cork.
(c) At times the uterine canal cannot be probed (in such instances, except for interstitial sources, radium must be limited to a vaginal application).
(d) When the uterus is small the three radium tubes composing the tandem may have to be reduced to two.
(e) Complications may arise as hyperpyrexia; radium must be removed before the planned time interval.

Radon seeds alone were inserted into the cervix but once in a case of cervical stump. She survived five and a half years before extension of the carcinoma resulted in death. Radium needles were inserted into the cervix and paracervical structures in 11 instances, usually in combination with tandem and colpostat, once in combination with seeds. Two women who were so treated with radium needles have survived to date, seven and six years respectively. Nine have died, surviving an average of thirteen months.

In reviewing the radium dosage, it was

decided to accept 4,800 milligram-hours with radium sources both in the uterus and vagina as a so-called therapeutic dose. A total of 94 women received this or a larger dose with 24 surviving—25 per cent. In 21 instances radium application was limited to the vagina (not including cases of cervical stump); just 1 of these women has survived, 5 per cent. Of the 34 women who received the so-called inadequate radium dose, namely radium in both uterine and cervical canals for less than 4,800 mg-hr., 6 survived, 17 per cent. Some in this latter group, however, had received an indeterminate radium application elsewhere before admission (Fig. 6).

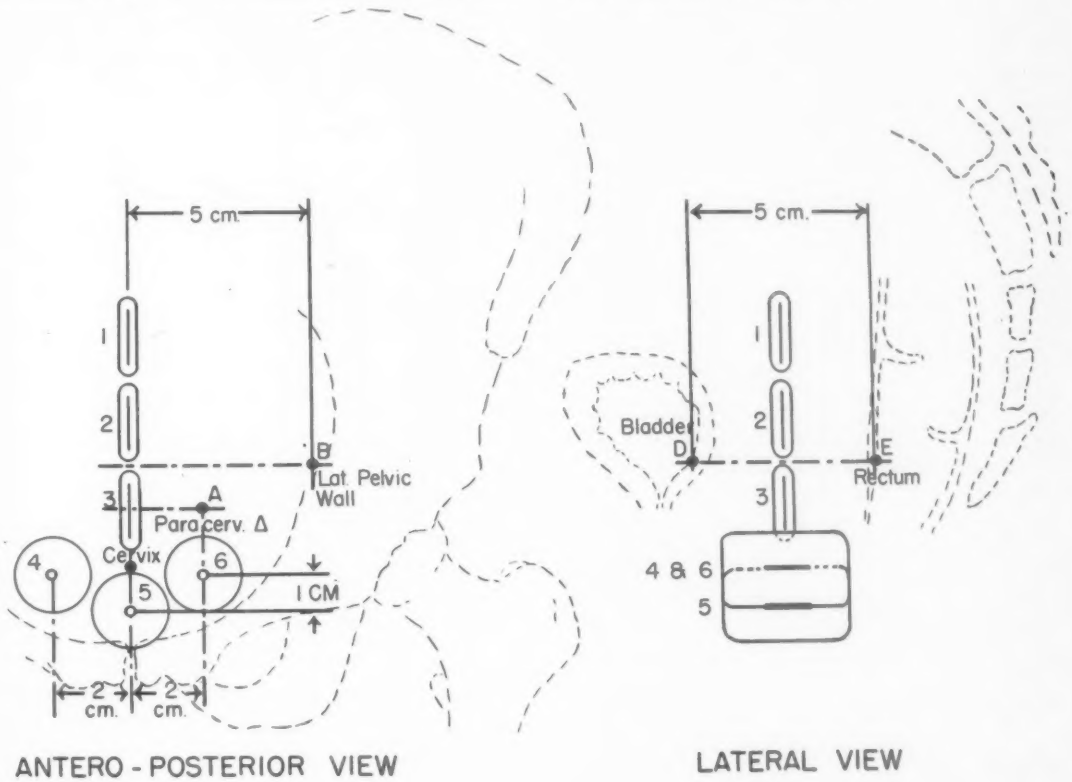


Fig. 7.

Following the publication of Sandler[12] an effort was made to ascertain radium dosage in gamma roentgens to certain fixed points within the pelvis. The following points were chosen (Howes):[7]

A—A point 2 cm. lateral to the center of the lower radium tube in the cervical canal. This is calculated as just lateral to the cervix at the base of the broad ligaments and marks the nearest point to the crossing of the uterine artery and ureter. This is designated as the paracervical triangle and represents the most sensitive location in the pelvis as to the limitation of tolerance of normal structures to radiation (Tod and Meredith[15]).

B—A point 5 cm. lateral to the interspace between the lower two tubes in the cervical and uterine canal and represents the position of the obturator node located within a centimeter of the lateral pelvic wall. Point B may also be thought of as a focal point within the lateral extension of the broad ligament. This is called the lateral pelvic wall.

C—A point ½ cm. below the tip of the lower tube in the cervical canal and at the apex of the circumference of the central cork within the vagina. This represents the external os and is called the cervix.

D and E—Points 2½ cm. anterior and posterior to the junction between the lower tubes in the uterine canal, designed as bladder, D, and

TABLE II

ROENTGENS PER MILLIGRAM-HOUR

Filtration Correction Factor — *0.5 mm. Pt. Filtration* — *Length of Tubes*
1 mm. plat. = 0.9 — Over-all 22 mm.
1.5 mm. plat. = 0.8 — Active 15 mm.
Figures in parentheses approximate — r per mg-hr.

Tube No.	A Paracervical Triangle	B Lateral Pelvic Wall	C Cervix	D Rectum or Bladder
1	0.27	0.23	(0.20)	0.46
2	0.90	0.31	(0.49)	1.07
3	1.92	0.31	(3.42)	1.07
4	0.42	0.14	1.59	0.53
5	0.67	0.19	7.10	0.36
6	2.23	0.46	1.59	0.55
Total	6.41	1.64	(14.39)	4.02
Average	1.07	0.27	(2.39)	0.67

This radium dosage distribution calculation was made by C. B. Braestrup, using dosage tables computed by Wolf.[17]

rectum, E. The bladder and rectum are of course, large mobile organs. D and E were computed as theoretically representing some near point in their wall and the dosage computed should therefore be considered the maximum gamma r delivered to these structures (Fig. 7).

With the radium sources so arranged Braestrup drew up the following tables specifying the gamma roentgens per milligram-hour delivered to these locations (Table II). Such tables can only represent a rough approximation of the actual gamma roentgens delivered in any one instance; as pelves vary in size and shape, no uterus ever lies in an exact central axial plane, the uterus being normally anteflexed on the long axis of the vagina at an angle of 90°. Unless the pelvis is frozen the angle of anteflexion or retroflexion will vary with filling and emptying of the bladder or rectum. In time the constant pressure of the colpostat against the walls of the va-

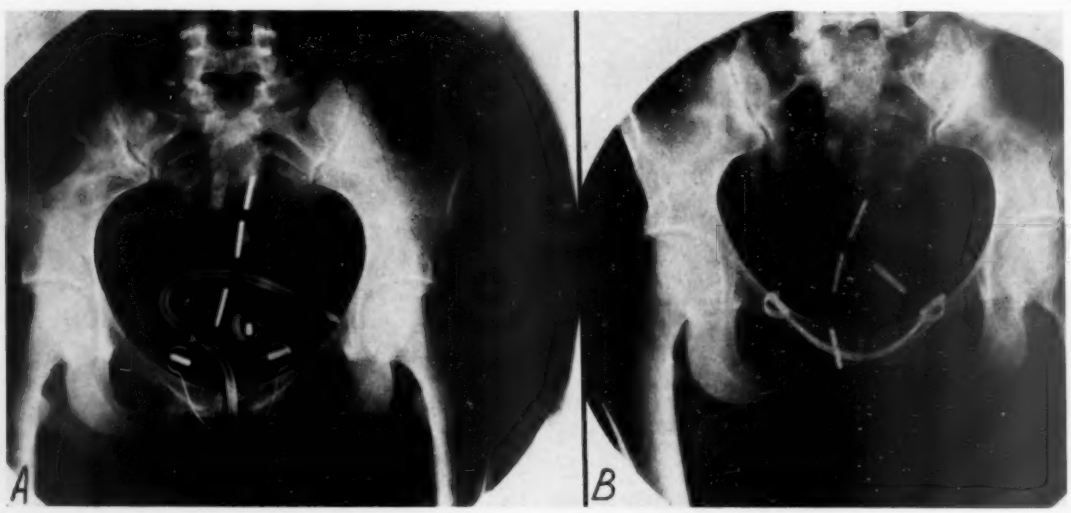


FIG. 8. *A*, arrangement of radium sources at time of insertion. *B*, arrangement of radium sources 100 hours later.

gina overcomes the normal tonicity of the vagina and allows the arms of the colpostat to spread (Fig. 8). Because of this tendency of the arms of the colpostat to shift, corks or ovoids would appear to be preferable to maintain the radium sources in constant position. To illustrate the use of these tables three radium tubes each of 10 mg. 1 mm. platinum filtration in tandem formation within the uterocervical and three sources of the same strength in the vagina, 1 mm. platinum filtration plus 1 cm. of rubber in the vagina; such a set when left in situ for 100 hours to give 6,000 mg-hr. will deliver the following doses to these predetermined locations:

A	B	C	D and E
Paracervical Triangle	Lateral Pelvic Wall	Cervix	Bladder and Rectum
5,769 r_γ $5\frac{1}{2}$ E	1,476 r_γ $1\frac{1}{2}$ E	12,951 r_γ 13 E	3,618 r_γ $3\frac{1}{2}$ E

Complications Incidental to Radium Applications.

Complications which may arise following such a radium application are well understood. For a discussion they are subdivided into those referable (*a*) to the intestinal tract, and (*b*) to the urinary system (Fig. 9 and 10).

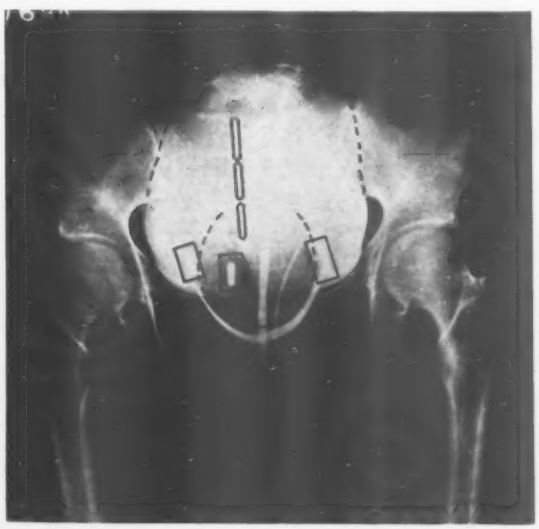


Fig. 9. Anteroposterior roentgenogram (opaque material filling bladder, air in rectum). Radium tubes drawn in for clarification to illustrate relationship of bladder and rectum to radium sources.

Fig. 10. Lateral roentgenogram (opaque material filling bladder and air in rectum). Posterior wall of bladder, dotted line. Cervical mass protrudes into air-filled rectum, double dotted line.

(*a*) *Rectum, sigmoid colon, cecum and ileum:* Diarrhea with passage of mucus and watery stools often follows removal of radium. If this diarrhea continues unabated for over two weeks there is danger that an ulcerating mucosal lesion may develop, "pseudocarcinoma of the rectum," as described by Todd.[16] With ulceration blood is added to the mucofecal discharges. In this series, 16 women are recorded as having long-continued diarrhea with blood and mucus in their discharge. In several instances this rectal ulceration was biopsied on the presumption that it represented a carcinomatous extension. Corscaden, Kasabach and Lenz[3] have brought out in this regard the significance of reducing the unit radium dosage and increasing the time of radium application, and in discussion giving their experience at the Presbyterian Hospital, they state: "Prior to that change [reducing unit strength in radium capsules]

there was 8.7 per cent of intestinal injury. Since that time there has not been a single intestinal injury" (Fig. 11).

Rectovaginal fistulas, on the other hand, are more frequently the result of carcinomatous extension. The carcinoma as it extends beyond the cervix involves the rectovaginal septum. In time, this neoplastic extension tends to break down, possibly due to the tumor outstripping its own blood supply along with infection, also as a result of radiation effect on the tumor. Rectovaginal fistulas were recorded in 14 instances; 2 of these patients developed in addition a vesicovaginal fistula. The fact that 2 women survived with colostomy over five years would suggest that in at least these instances the fistula was not the result of tumor extension.

Both cecum and ileum may drape over the pelvic inlet and lie in close proximity or be adherent to the uterus. Thus they are exposed to the effects of concentrated radiation. This series records 6 colostomies and 2 ileostomies which were performed to relieve the distressing complications of treatment and disease to ileum or cecum.

(*b*) *Bladder, uterus and kidneys:* According to Ewing,[5] "The natural termination of most cases of uterine cancer is through uremia from occlusion of the ureters." Martin and Rogers[11] demonstrated how the effects of unfiltered radium in close apposition to the ureter will result in ureteral obstruction. With filtration, however, they state that the ureter will withstand at least 2.5 erythema doses without ill effect. Jaffe, Meigs, Graves and Kickham[8] write that in their series no cases of Group 1 or 2 developed hydronephrosis or hydroureter. Two of their cases classified as Group 3 developed partial ureteral obstruction, seven to twenty-one months after irradiation. Both recovered after ureteral dilatation, suggesting that in these 2 instances the obstruction may have resulted from replacement fibrosis. In this series, it is felt that the ureteral stricture was in most instances due to choking off of the ureter by massive growth of carcinoma. This stricture was found to be irreversible and not influenced by catheterization and dilatation or additional radium or roentgen therapy. Leucutia[9] states that no treatment has as

Fig. 11. Narrowed segment upper rectum, complication secondary to radium application.

yet been arrived at which can be deemed successful in overcoming this complication. In this series 43 individuals, 19 per cent, are listed with a non-functioning kidney, advanced hydronephrosis and hydroureter or with pyonephritis. This enumeration, however, is incomplete as many patients did not return for follow-up examinations but were followed through home contact by the Social Service Department.

Women do not bear the unpleasantness and discomfort of nephrostomy or ureteral transplantation to the skin as philosophically as men. But 1 woman in this series had both ureters transplanted to skin; she died within nine months. Transplantation to bowel is associated with a high operative mortality. Of 2 who had the ureters so transplanted, both died; 1 lived three months, the other three years. Three were nephrostomized for impending uremia, and lived for only a short time thereafter. Seven were treated by nephrectomy, 1 of whom is still living over six years. The average survival following nephrectomy was three and a half years, illustrating the advantage of nephrectomy in carefully chosen cases (Drexler and Howes[4]).

Bladder mucosa is not as frequently involved by advancing carcinoma or radiation injury as the rectum. This may be from lack of proper interpretation of the findings as frequency and urgency commonly follow radium removal. Hematuria is often masked by the presence of bloody vaginal discharge. Necrosis of bladder mucosa (post-irradiation) was listed in 4 instances, 1 at autopsy. Calcific encrustation should make the observer suspicious of radiation ulcer. This necrosis was found to be delayed from several months to over a year after irradiation. The urologist frequently reported lifting of the bladder floor and the presence of bullous edema, interpreted as evidence of carcinoma extension rather than radiation reaction. The bladder was marsupialized once and an unsuccessful attempt made to destroy the carcinomatous extension by direct irradiation using contact roentgen therapy; later radium tubes were applied. A more critical analysis of these bladder complications is indicated.

Fig. 12. Pigmentation of skin to illustrate location of lateral portal.

Behney[2] has shown that vesicovaginal fistulas may occur even more frequently in untreated than in treated cases. Fourteen women developed vesicovaginal fistulas which in all but one case appeared to be the result of carcinoma extension. The exception was that of W. K., a young woman; repeated biopsies of her fistulous tract were always reported as negative for carcinoma. She left the state and was lost after four years of follow-up.

III. *Roentgen Therapy.* Throughout 1936 roentgen therapy was delivered routinely through four portals. At that time the total dosage to each skin area was increased from 1,600 r to 2,400 r (in air). After careful deliberation it was decided that this technique did not deliver adequate dosage to the outer pelvis. Lateral fields were therefore added to augment the two anterior and two posterior portals. This roentgen technique was carried out using two anterior, two posterior and two lateral portals throughout 1937 and 1938 (Fig. 12).

Complications Following Roentgen Irradiation to Lateral Pelvis. In 1939 three

patients reported back with pathological fracture of the femoral neck (Strauss and McGoldrick[14]). Upon realization of the significance of this complication the lateral fields were discontinued and the pelvis was crossfired by three anterior and three posterior portals (Fig. 13, *A* and *B*). Since eliminating the lateral portal not a single fracture of the hip has occurred.

Present Methods of Roentgen Therapy. Most women have a sufficient transverse pelvic diameter to accommodate three portals 10 cm. in width anteriorly and a similar number posteriorly. With women of smaller dimensions the width of the portals may have to be cut down to 8 cm. Fifteen centimeters is used routinely as the vertical diameter, this to extend the irradiated block from the iliac crests to the horizontal rami of the pubic bones. The dosage to each skin portal varied from 2,400 r to 3,000 r (in air); this in an effort to deliver 4,500 r to each parametrium calculating crossfire from four portals (Fig. 14, 15 and 16). After such an extensive cycle of roentgen irradiation difficulty was encountered in inserting the planned radium. The vagina had frequently contracted and as a result it became difficult to insert three radium corks into the vaginal vault, or the cervical os had closed and, with the fibrotic post-irradiation changes, difficult to dilate. In view of these difficulties it was agreed to divide the roentgen-ray cycle, giving from one-third to one-half the proposed roentgen radiation, then interrupting for radium treatment. This smaller dose cuts down infection and tendency to bleed without causing the contractures secondary to more extensive roentgen treatment. Roentgen therapy is then recommenced from one to two weeks after the radium is removed and the balance of the therapy completed. Recently this latent period before re-instituting roentgen therapy has been shortened to a few days. Then, too, the central portals, both anterior and posterior, have been divided by a lead strip up to 2 cm. in width thus saving the pelvic structures which lie in the midline (bladder and rectum) from such intensive roentgen irradiation in addition to radium radiation.

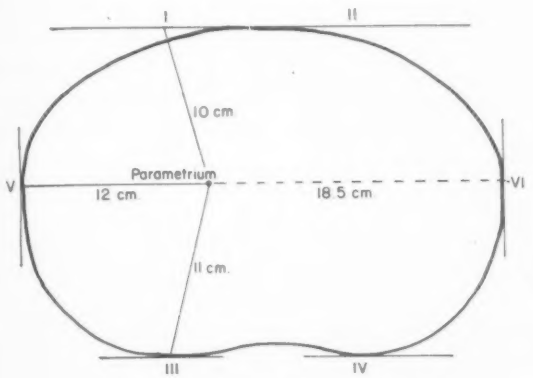
FIG. 13. *A*, pigmentation and peeling to illustrate type of skin reaction and location of portals following pelvic cycle to deliver estimated 5,500 r into parametria. *B*, posterior view.

As an aid to prevent injury to the small intestine, all patients are treated in the Trendelenburg position. This position does not dislodge all the ileal loops out of the pelvis as can be accomplished with pneumoperitoneum, but this positioning in some ways does reduce morbidity (nausea, intestinal cramps and diarrhea).

Addition of Perineal Field. A perineal field was frequently added in the years 1936

through 1938. The perineal tissues will not tolerate over 1,000 r (in air) without producing an uncomfortable skin reaction. This portal was discontinued after calculation that only 10 per cent of the surface dose reaches the depth of the paracervical tissues. No individual receiving this perineal portal survived.

Intravaginal Roentgen Therapy. Direct roentgen irradiation by way of intravaginal cone was used instead of and to augment radium therapy in chosen cases. Seventeen women received such direct intravaginal irradiation up to 4,000 r (in air). Four of these, nearly 25 per cent, are still living, all over seven years. Two of these survivors are cases of carcinoma in the cervical stump. All but one of these survivors received additional intraluminal radium therapy. Ten other women received smaller doses of intravaginal roentgen irradiation of from 800 to 3,000 r. No survivors are

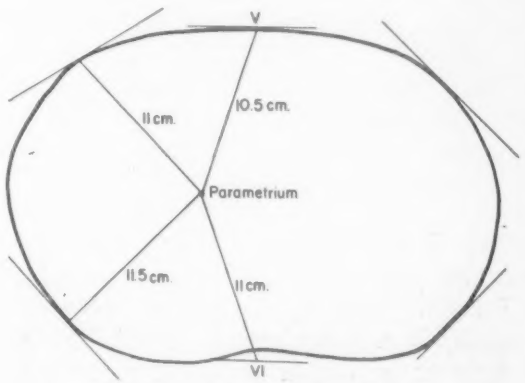


Cross Section of Pelvis, 20 cm x 30 cm
200 KV, 0.5 mm Cu, 1 Al, TSD 50 cm

Depth Dose to Parametrium, Rt. Side

Port	I	II	III	IV	V	VI	Total
Dose/100r per port	44		39		35	17	135 r
Dose/3000r per port	→ 4050 r						

FIG. 14. Pelvis 20 by 30 cm. using two anterior and two posterior and two lateral portals; dose to parametria calculated 4,050 r.

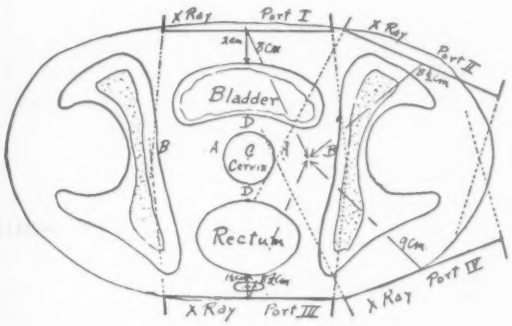


Cross Section of Pelvis, 20 cm x 30 cm.
200 KV, 0.5 mm Cu, 1 Al, TSD 50 cm.

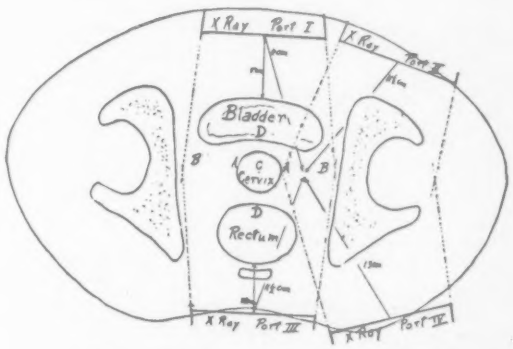
Depth Dose to Parametrium, Rt. Side

Port	I	II	III	IV	V	VI	Total
Dose/100r per port	39		37		41	39	156 r
Dose/3000r per port	→ 4680 r						

FIG. 15. Pelvis 20 by 30 cm. using three anterior and three posterior portals, dose to parametria is increased to 4,680 r, all other factors remaining the same.



Schematic cross section of pelvis 16 cm. in diameter.



Schematic cross section of pelvis 23 cm. antero-posterior diameter (with compression)

FIG. 16. Pelvis 16 cm. anteroposterior diameter, 2,000 r (in air) is necessary to deliver 4,500 r to parametria. Pelvis 23 cm. anteroposterior diameter, 2,600 r (in air) is necessary to deliver 4,500 r to parametria.

listed among those receiving the smaller intravaginal dose.

Estimated Dosage to Parametria. The importance of delivering adequate irradiation into the region of the parametrial structures has been emphasized by Frazell.[6] By using three anterior and three posterior portals a tumor dose of 4,500 r can be delivered to the parametria. To this is added from 5 to 1.5 erythema doses delivered by gamma radiation to the paracervical triangle and the lateral pelvic wall. The equivalent of 13 erythema doses (paracervical triangle) and 9 erythema doses (lateral pelvic wall) has been accumulated to these parts by these two modalities usually in a two month interval. The proportionately higher survival rate in the latter three years of this study, 1939, 1940, 1941, is ascribed to this plan of treatment.

SUMMARY

1. Two hundred thirty cases with a proved diagnosis of carcinoma of the cervix admitted to the Brooklyn Cancer Institute in the years 1936 through 1941 inclusive are studied. This allows a follow-up of from eleven to five years.

2. Classification is made as to race, age incidence, and number of pregnancies. Survival from a pathological and clinical classification is tabulated.

3. The method of treatment is summarized with discussion of the end results and complications, weighed against the particular therapy received.

4. The larger percentage of survivors appears to have been obtained when radium dosage is delivered up to 5.5 erythema doses into the region of the paracervical triangle (parametrium). This is augmented by additional roentgen irradiation approximating 7 erythema doses.

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TRACHEAL DIVERTICULA

REPORT OF A CASE

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A DIVERTICULUM of the trachea is a rare abnormality which is not without potential serious complications. Kernan[4] reported a case of a two month old infant in whom a tracheal diverticulum had eroded into the innominate artery. Infection of a diverticulum of the trachea may be a source of pulmonary infection; abscess formation and even rupture into the mediastinum are possibilities. By compression or traction the recurrent laryngeal nerve may be paralyzed.[10]

As far back as the Fifth Century, Aetius noted aerial goiters which formed in the neck after parturition. Plater,[7] in the Seventeenth Century, described tracheal diverticula and differentiated them from goiter. In 1846, Rokitansky[8] described the condition and postulated that they resulted from coughing due to chronic pulmonary or bronchial disease. The first case report was presented by Mackenzie[3] in 1911. Diverticula of the trachea, of considerable size, were described in Egyptian minaret criers and in drill sergeants.[10]

The condition unfortunately does not lend itself readily to clinical diagnosis. By far the great majority of cases is discovered at autopsy, although Addington, Rusk and Cohen[1] described a case in which a saccular tracheal diverticulum (5 by 4 by 5 cm.) was diagnosed from a bronchogram. In the differential diagnosis, esophageal diverticulum and tracheal retention cysts must be eliminated. Ziegelman[10] recommends tracheograms after the instillation of iodine in poppyseed oil into the trachea, with the patient in a modified Trendelenburg position.

Tracheal diverticula are of congenital or acquired origin and the latter group may be subdivided into traction or pulsion types. Stibbe[9] believed that the congenital form has a narrow opening, contrasted with the large opening of the acquired form. Chiari[2] thought congenital diverticula are prone to develop at the site where accessory bronchi are most likely to be found. He mentioned Petit's[6] belief that it is possible that the diverticula may be only potential, and that prolonged, increased intratracheal pressure is required to develop them.

In a study of tracheal anatomy, Miller[5] described the trachealis muscle as consisting of transverse bands which unite with the cornua of the cartilage semi-rings. Between these muscle bands are amuscular and relatively weak areas. Except for a reported case in which the patient was found to have a diverticulum due to a rupture of three tracheal semi-rings after a blast explosion, almost all diverticula of the trachea occur on the posterior wall. Undoubtedly, chronic increased intratracheal pressure is an important factor in the production of this condition.

Frequently other pulmonary or bronchial disease is associated, particularly cystic disease of the lung and bronchiectasis. That there may be an inherent susceptibility or weakness of the tracheal wall which, coupled with infection and chronic cough leads to the production of diverticula, is a likely possibility. True congenital diverticula of the trachea are uncommon.

REPORT OF A CASE

H. G., male, aged sixty-six, of Norwegian extraction, was admitted to the Municipal Tuberculosis Sanitarium of Chicago, November 14, 1945. His chief complaints were dyspnea, weakness and a 12 lb. (5.4 kg.) weight loss.

At the age of thirty-three the patient fell against a picket fence with enough force to lead him to believe that a picket pierced his right

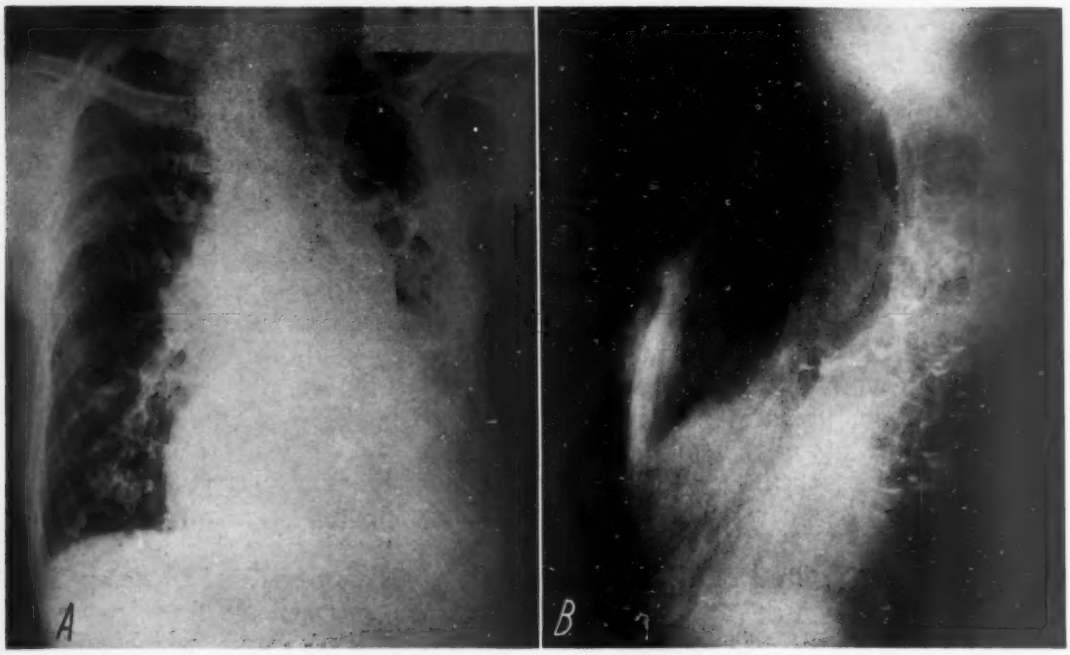

FIG. 1. Anteroposterior (*A*) roentgenogram of the chest and bronchogram (*B*), lateral view. The cystic disease of the right lung is well outlined in both films.

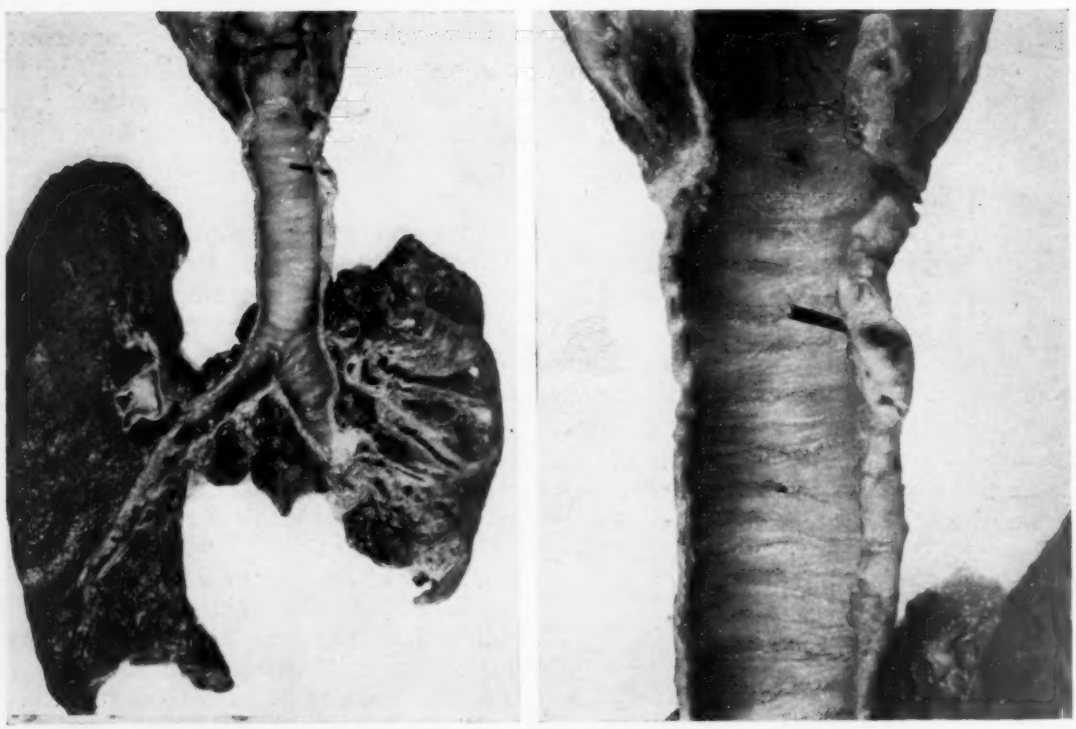

FIG. 2. Photographs of the lungs and trachea after section. The right lung is contracted and cystic. The transversely sectioned diverticulum contains a probe and lies immediately below the smaller diverticulum.

chest wall. Pneumonia developed promptly in the presumably injured lung. The course was protracted and complicated by a considerable pulmonary hemorrhage. He felt well since his recovery until June, 1945, when he began to feel tired, though able to continue his work. In October, 1945, his second pulmonary hemorrhage forced him to rest.

His family history was not significant.

Examination. The patient was 5 ft. 4 in. tall, weighed 102 lb. (46.3 kg.). The pulse was accelerated but regular. The systolic pressure was 130, the diastolic 68, the temperature was 100.6°F. He was dyspneic and pale. The fingers were clubbed; the chest was narrow and asymmetrical with some restriction of movement on the right. In the right upper half there was impaired resonance, amphoric breath sounds and many moist rales; throughout the left chest were many mixed rales. The vital capacity was 900 cc. All other physical findings were normal.

A roentgenogram of the chest showed cavitation in the upper half of the right lung with partial atelectasis in the right base. The heart and mediastinum were shifted to the right. The left lung was normal except for a thickened apical pleura. A bronchogram revealed marked saccular dilatation of the right middle lobe bronchioles.

The hemoglobin was 62 per cent and there were 4.1 million red blood cells. The white blood cell count was 9,100, with a normal differential. The sedimentation rate was 25 mm. in thirty minutes (Cutler). The Mantoux test (1:100 old tuberculin) was positive. The urine contained 200 mg. albumin and a few red cells. Repeated sputum examinations were negative for tubercle bacilli.

After a few days the patient became afebrile and was discharged five weeks after his admission. The diagnosis was cystic disease of the right lung with superimposed, nonspecific infection.

Second Admission. The patient was readmitted on October 24, 1946, complaining of dyspnea, weakness and difficulty in urination. He had been resting at home since his discharge.

Examination. The blood pressure was 120 systolic and 80 diastolic and the temperature 99.8°F. The pulse rate was irregular. In addition to the previous chest findings there was some dullness and rales in the left base. An electrocardiogram disclosed auricular premature systoles. Other laboratory findings were unchanged from those of the previous admission.

Fig. 3 Photomicrographs (15× and 125×) of the diverticulum wall. The epithelium is ciliated columnar and there is a scattered round cell infiltration. Peripheral to the fibrous tissue is a normal mucous gland.

With penicillin therapy (30,000 units every three hours, intramuscularly) he improved and was discharged November 16, 1946.

Final Admission. December 6, 1946. The patient was now markedly dyspneic. On examination the heart sounds were distant and absolutely irregular. The liver extended 5 cm. below the left costal margin and was slightly tender and smooth. Both lungs contained many loud, moist rales in both bases. Cyanosis was marked.

A roentgenogram of the chest showed no

change compared to his previous films. The red and white blood cell counts were unchanged from those of his first admission. Four days before his death the white blood cell count rose to 14,370, with 77 per cent polymorphonuclear leukocytes. The urine contained 100 mg. of albumin and a few red cells. Sputum examinations were persistently negative for tubercle bacilli.

Digitalis therapy was instituted. He became febrile (101°F.), progressively weaker and short of breath. Death occurred December 11, 1946.

Autopsy (two hours after death). The body was that of an emaciated white man about sixty-eight years old. The chest was fairly symmetrical and without evidence of old injuries. The entire right lung was adherent to the chest wall while the left lung was free in the pleural space. Somewhat shrunken, the right lung on section contained many smooth, fibrous walled cysts which ranged from 2 cm. to 10 cm. in diameter. Between these air-filled cysts the lung parenchyma was compressed and minimal in amount. The bronchi were dilated and their walls somewhat thickened. Purulent exudate was minimal.

The left lung was pale and spongy throughout; the bronchial tree was normal. In the apex a 2 cm. fibrous scar was found.

On the right posterolateral aspect of the trachea, 2.5 cm. distally from the larynx and 3 mm. from the cornua of the fourth and fifth cartilage rings respectively were two openings large enough to pass a small probe. Each communicated with an air-filled diverticulum, the first of which measured 0.5 cm. in diameter and 1 cm. in length. The second diverticulum, situated 1 cm. from the first, measured 1 cm. in diameter and 1.5 cm. in length. There were no adhesions and the trachea was otherwise normal.

The heart weighed 300 gm. It was essentially normal except for dilatation of the ventricles, especially the right. The ascending aorta contained numerous, large, yellow plaques.

The spleen weighed 120 gm. The capsule and parenchyma were studded with numerous (3 mm. in diameter) yellow nodules. These contained caseous centers and were well encapsulated.

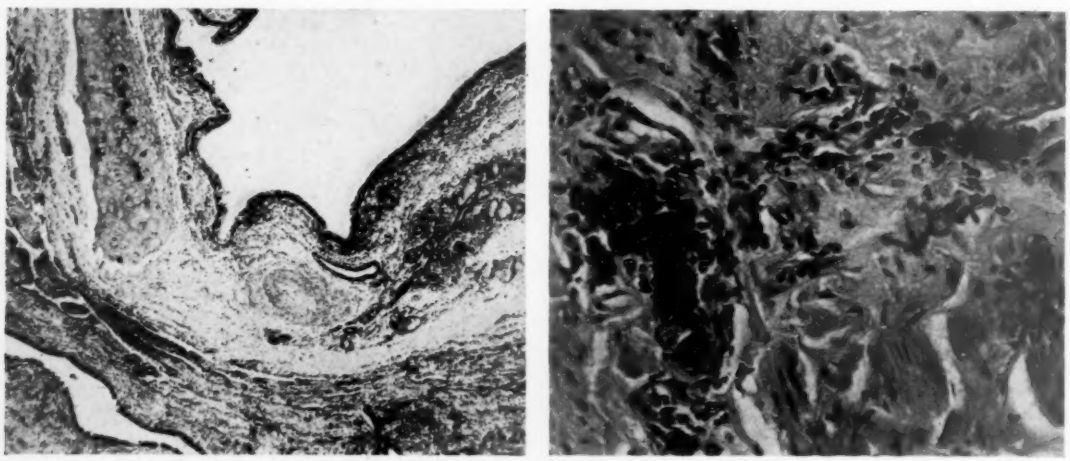

FIG. 4. Photomicrographs (10× and 240×) of a cyst wall and of the moderate anthracosis in the cystic lung. There is an orderly arrangement of cartilage, smooth muscle and mucous glands.

The liver weighed 1,700 gm. It extended 8 cm. below the level of the costal margin. On section the vascular markings were prominent on a yellow background. Four small, yellow nodules were discovered.

The kidneys weighed together 320 gm. They were congested and contained a few thin-walled retention cysts. In the right kidney a 2 mm. firm, yellow nodule was found in the cortex.

The remaining organs showed no significant changes.

Microscopic Examination. The diverticula were lined with stratified columnar, ciliated epithelium which rested on a fairly distinct basement membrane. The submucosa was of loose areolar tissue and, in areas, infiltrated by lymphocytes. The greater part of the wall was

composed of fibrous tissue, at the periphery of which a post-tracheal mucous gland was found. The blood vessels were not remarkable.

In the right lung the epithelium of the cysts ranged from ciliated columnar to stratified squamous. Occasionally a cyst wall was ulcerated and active inflammation was associated. Fibrous hyperplasia was marked. Anthracotic pigment was in considerable quantities. The few alveoli that were spared showed interstitial fibrosis. The bronchi were dilated and in some cysts there was an orderly arrangement of cartilage, smooth muscle, and mucous glands. Many of the cysts communicated with the bronchi. No evidence of malignant change was noted.

Anatomic Diagnosis. 1. Cystic bronchiectasis of the right lung with pleural fibrosis. 2. Tracheal diverticula. 3. Nephrosclerosis. 4. Healed tuberculous lesions of the spleen, liver, kidney and left lung. 5. Emphysema of the left lung. 6. Atherosclerosis of the aorta and coronary vessels. 7. Hypertrophy and dilatation of the right ventricle.

DISCUSSION

It is common to find associated anomalies in congenital cystic disease of the lungs and in this case, because of the tracheal anomalies, the pulmonary cystic disease could be considered as congenital. However, that premise is not well founded. The history of the patient revealed a chest injury followed by pneumonia; in addition, much coal pigment was found throughout the deep tissues where it had lodged when the alveoli were functioning. Whether a hereditary weakness of the bronchial structures was present, or whether a part of the cystic disease was congenital, could not be determined.

SUMMARY

Diverticula of the trachea are rare anomalies which are seldom diagnosed clinically. They may be of congenital or acquired origin and sometimes coexist with chronic pulmonary or bronchial disease. Potential complications are infection, abscess formation, rupture, and pressure (or traction) effects upon the recurrent laryngeal nerve. A case is presented having two tracheal diverticula which were found at autopsy. In the right lung, cystic bronchiectasis was marked and apparently of acquired origin.

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HEMANGIOMA OF THE KIDNEY

ITS ROENTGEN DIAGNOSIS

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HEMANGIOMA of the kidney is a rare lesion; there are less than 50 case reports in the literature. In both its clinical and roentgenologic manifestations, it may closely resemble renal carcinoma. Because of this similarity, it is desirable to emphasize such differentiating points as exist.

Hemangioma occurs in the kidney as an isolated lesion or as a manifestation of a generalized hemangiomatosis. They may be single or multiple. They are of the capillary or cavernous type. They may be located in the cortex, medulla, tip of a papilla or subepithelially in the renal pelvis. The majority are adjacent to the renal pelvis. They may vary in size from a few millimeters to several centimeters in diameter. When the pelvic epithelium is penetrated, hematuria results from rupture of one of the dilated vessels. If rupture of a vessel occurs within the tumor, a blood cyst may result.

FIG. 1. Case 1.

In 85 per cent of the reported cases, the onset of symptoms occurred before the age of forty. This is a distinguishing feature from renal carcinoma—its clinical onset is largely after the age of forty. The most constant symptom is hematuria. This may have been present intermittently for several years. In some cases, it may be so profuse as to require immediate surgery. Colicky pain is present in about 40 per cent of cases. This is usually due to the passage of blood clots. Nephrectomy is usually necessary for cure, though in some cases heminephrectomy has been performed.

The following 2 cases illustrate the salient features of this lesion.

REPORT OF CASES

CASE 1. On March 25, 1946, the patient, a white female, aged forty-nine, had an attack of acute left lumbar pain radiating to the umbilicus, of several minutes' duration. There was an accompanying hematuria. On March 29, 1946, the hematuria recurred. Past history was not relevant. Physical examination was negative. On March 29, cystoscopy revealed bloody urine in the bladder, with normal renal function bilaterally. Left retrograde urography (Fig. 1) revealed pyeloparenchymatous extravasation from the fornix of the left middle calix. The fornix was compressed and elongated as if by a soft tissue mass. The adjacent infundibulum was minimally compressed on its superior aspect. Throughout its distal two-thirds there was a homogeneous filling defect suggestive of blood clot. Lateral view revealed no renal displacement. On April 3, excretory urography (Fig. 2) revealed bilateral good function, with inadequate visualization of the left middle calix. On April 5, 1946, the patient was readmitted to

the Jewish Hospital. Smear and culture of the urine revealed no evidence of tubercle bacilli. Roentgen examination of the chest revealed thickened pleura at the left base.

On April 12, 1946, a left nephrectomy was performed. The kidney measured 10.5 by 2.5 cm. The middle calix was obstructed, with a submucous hemorrhage present in the adjacent pelvis. An angioma measuring 1.2 by 0.9 cm. was demonstrated in the kidney around the middle calix. Microscopic section revealed it to be a cavernous hemangioma impinging upon the

Fig. 2. Case I.

pelvis, and with a fine channel leading from it to the adjacent hyperplastic pelvic epithelium.

Case II. On March 14, 1946, this patient, a female, aged fifty-six, experienced an attack of left lumbar pain, nausea and vomiting, accompanied by the passage of bloody urine. In 1942, a similar episode occurred; she had considered the bleeding vaginal. In 1932, radium sterilization had been performed because of functional uterine bleeding. Physical examination revealed only hypertension with a blood pressure of 190/100.

On March 20, left retrograde urography was performed. It demonstrated (Fig. 3) deformity of the superior major calix. The infundibulum was widened, with a poorly defined defect present through its major portion. The fornix was compressed and elongated. There was increase in the width of the upper pole extracaliceal tissue, indicating the presence of a soft tissue mass. Lateral view revealed no displacement of the kidney. There was the incidental demonstration of increased concavity of one inferior caliceal fornix. On March 25, excretory urography revealed reduced function of the left kidney; right renal function was natural.

Fig. 3. Case II.

On April 5, 1946, a left nephrectomy was performed. The kidney measured 11.5 by 5 by 4 cm. The superior major calix was minimally dilated. A circular soft tissue mass, measuring 1 cm. in maximum diameter, projected into it. This mass contained fluid blood and blood clots, and surrounded a large vessel and numerous smaller vessels. Microscopic section through this mass demonstrated a cavernous hemangioma. In addition, a minute cavernous hemangioma was demonstrated on the surface of the kidney.

DISCUSSION

These 2 cases exhibit striking similarity in roentgen manifestations. In both cases there was evidence of a compressed fornix of a major calix, with deformity of the infundibulum and filling defect throughout its major portion. It is therefore suggested that when these roentgen manifestations are demonstrated in a patient under forty complaining of slight or recurrent episodes of hematuria, accompanied by renal colic,

the diagnosis of renal hemangioma should be strongly considered. It is unsuual that both these patients are over forty years of age. In a percentage of cases, however, early in the development of the lesion, roentgenologic examination is negative. When this occurs in a patient with unexplained hematuria, periodic roentgen examinations are indicated. The lesion may become demonstrable at a later date.

Nephrectomy or heminephrectomy is the treatment of choice.

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Philadelphia, Pa.

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Vol. 60, No. 3

CALCIFICATION IN THE OBLITERATED DUCTUS ARTERIOSUS OF AN INFANT*

A VERIFIED EXAMPLE DIAGNOSED BEFORE DEATH

CASE REPORT

By WILLIAM J. ELLIOTT, M.D., *and* ARTHUR E. CHILDE, M.D.

WINNIPEG, MANITOBA

THE roentgenographic demonstration of calcification in the obliterated ductus arteriosus was reported by Childe and MacKenzie[1] in 1945. Their material consisted of 4 cases, 1 discovered at postmortem examination and 3 others in whom chest roentgenograms revealed shadows which were considered to represent calcium in the ductus arteriosus. Unfortunately, in their verified case there had been no roentgenogram of the chest before death, although examination of the heart after removal showed quite dense calcification which should have been readily recognizable during life. The present case is being reported as it represents an example of calcification in an obliterated ductus arterio-

[1] Childe, A. E., and Mackenzie, Eleanor R. Calcification in the ductus arteriosus. Am. J. Roentgenol. & Rad. Therapy, 1945, 54, 370–374.

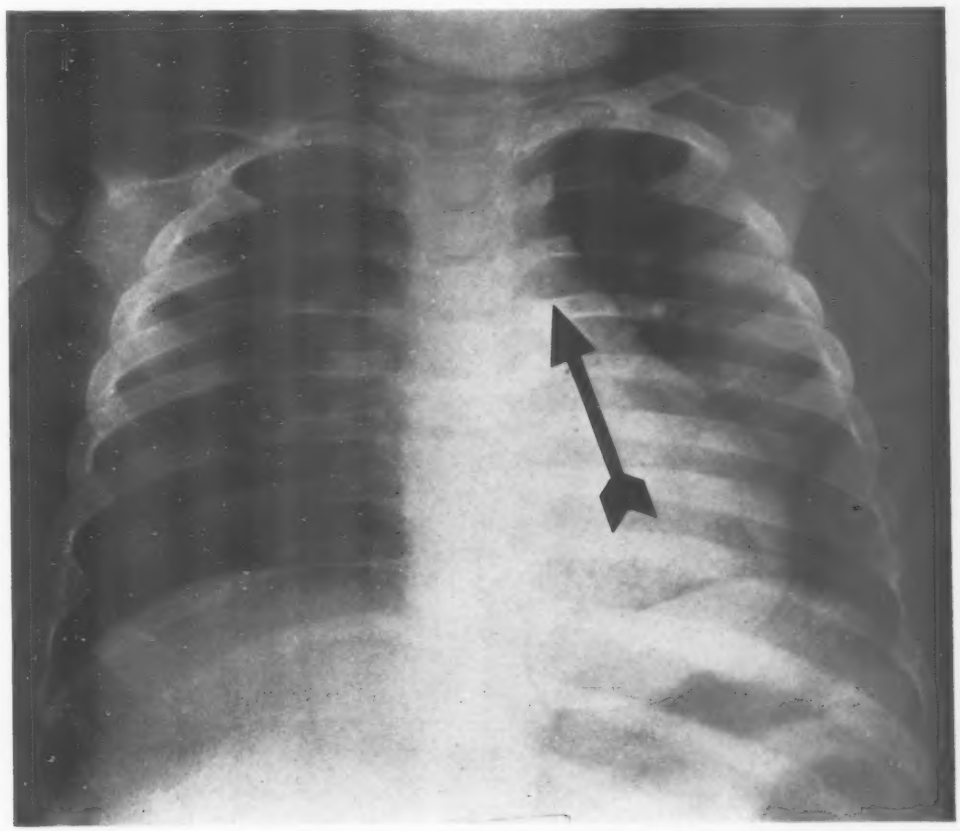

Fig. 1. Posteroanterior roentgenogram of the chest made shortly before death. The calcified obliterated ductus arteriosus lies close to the point of the arrow opposite the fourth interspace posteriorly.

* From the Department of Roentgenology, The Winnipeg General Hospital, Winnipeg, Manitoba.

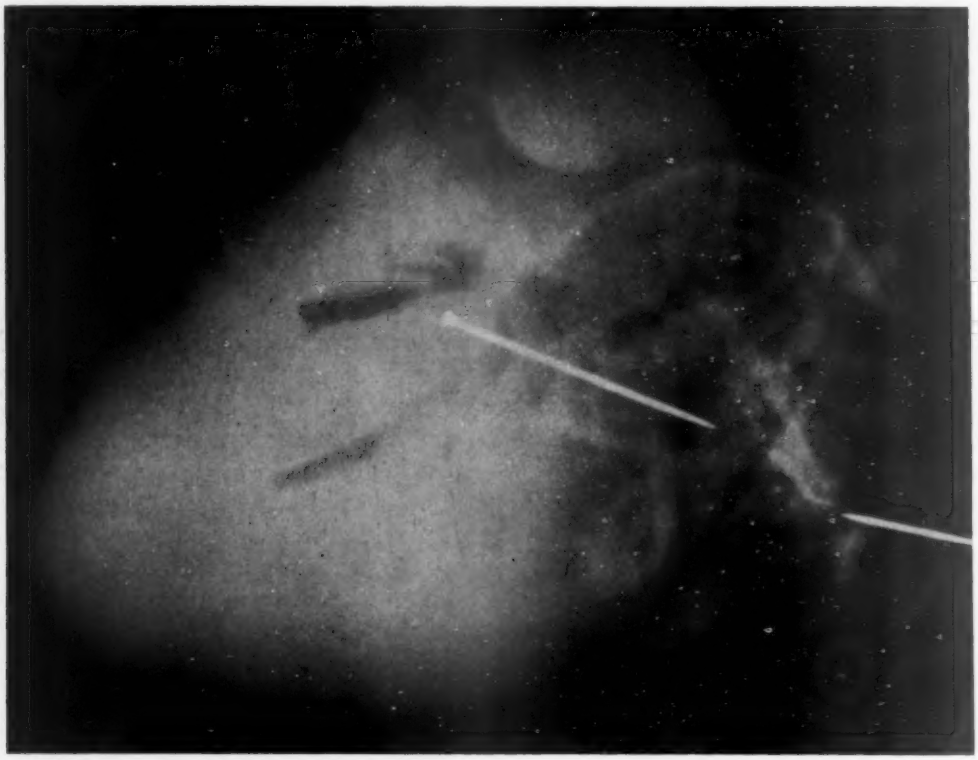

FIG. 2. Removed heart and great vessels. The ductus arteriosus lies between the points of the pins and the calcification can be seen to be chiefly in its aortic half.

sus visible in a roentgenogram of the chest of an infant and verified the same day by postmortem examination.

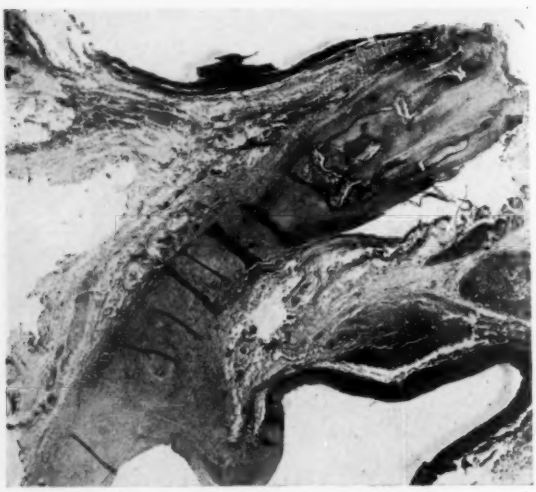

FIG. 3. Longitudinal section through the ductus arteriosus. The dimple in the pulmonary artery is shown at the lower left and aortic termination at the upper right. (Hematoxylin and eosin ×7.)

CASE REPORT

J. D. (Autopsy No. A-6059). This white female child was first admitted to the Winnipeg General Hospital at the age of fifteen and a half months suffering from severe nutritional anemia. The family background was bad, six other siblings all having suffered from "anemia" in infancy. Her diet had consisted of nothing but an inadequate milk formula plus a few scraps of food from the table. With increased nutrition, small transfusions and iron and liver therapy her erythrocyte count rose from 2.29 to 4.89 million per cu. mm. and her hemoglobin from 29 per cent to 79 per cent in one month. She was readmitted at the age of nineteen months with a history of a "cold" for one month and convulsions for twelve hours. Examination showed her to be comatose. Her neck was not rigid and Kernig's sign was negative. There was some question of blowing breathing in the left lung, and consequently roentgenograms of the chest were made on her way up to the ward. These showed no infiltration in either lung but in the posteroanterior projection there was seen a shadow with the density of calcium

measuring 3 by 1 mm. situated just to the left of the vertebral column opposite the fourth interspace posteriorly (Fig. 1). This was not visible in the lateral view. Nothing otherwise remarkable was noted.

She died two hours after admission and an autopsy the same afternoon showed the cause of death to be pneumococcal meningitis. In view of the roentgenological suggestion of calcification in the ductus arteriosus a careful dissection of the heart and great vessels was made. The ductus was found to be hard and a roentgenogram of the removed specimen confirmed the presence of calcification in this structure (Fig. 2). Microsection through its long axis after partial decalcification showed the lumen to be completely obliterated by fibrous connective tissue containing a small amount of elastic tissue. Scattered through the partially hyalinized connective tissue and chiefly in the aortic half of the ductus there was amorphous granular basophilic staining calcium deposit (Fig. 3 and 4).

SUMMARY

This case report describes an example of calcification in the obliterated ductus arteriosus of an infant nineteen and a half months of age, suspected from a roentgenogram of the chest and verified later at postmortem examination.

FIG. 4. Higher magnification of aortic portion of the ductus arteriosus showing dark staining calcification. Calcium has been dissolved from the irregular spaces during preparation of the specimen. (Hematoxylin and eosin ×30.)

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UNDISTORTED VERTICAL PROJECTIONS OF THE HEAD FROM LATERAL AND POSTERO-ANTERIOR ROENTGENOGRAMS*

By WENDELL L. WYLIE, D.D.S., M.S., *and* W. A. ELSASSER, A.B., D.D.S.†
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THE most precise instrument yet devised for the quantitative study of craniofacial morphology is the Broadbent-Bolton roentgenographic cephalometer. Since it has been adequately described elsewhere in the literature, no extensive review of its design will be given here. The apparatus consists of a head-holding device to maintain the subject's head in the Frankfort plane, and two roentgen-ray heads fixed in relation to the head-holder so that the central ray of one (lateral) passes through both external auditory meati, entering from the right side, with the other (posteroanterior or frontal) at right angles to the central ray of the lateral tube, passing along the intersection of the median sagittal and Frankfort planes of the subject. Rods in the earholes and a rest at the bridge of the nose stabilize the patient's head. Appropriate channels are provided for cassettes so that true lateral and frontal views may be taken at right angles to one another.

A factor which must be recognized in all roentgenographic techniques, and particularly those in which quantitative measurements are to be made, is the divergence of the rays as they leave the anode. The Broadbent instrument minimizes the resultant size distortion in the image by having the films as close as possible to the subject's head, and by locating the anode as far as is practicably possible from the subject's head. This does not eliminate size distortion, however, and consequently vernier scales are provided whereby one may read to one-tenth of a millimeter the distance from the median sagittal plane to the lateral film, and the distance from the posteroanterior film to the ear-rod axis. Since the distance from the median sagittal plane to the lateral anode and the distance from the ear-rod axis to the posteroanterior anode is exactly 5 feet, all necessary values are known for accurate computation of true dimensions from the distorted ones in the films, using the method of similar triangles.

In the decade and a half in which the Broadbent cephalometer has been used, the lateral head film has received more attention than has the frontal. This reflects not only primary interests of investigators, but also the fact that problems of size distortion in the lateral view are inconsequential enough that they may usually be ignored. This is not true of the frontal, however, and it seems safe to say that if an acceptable method for correcting for size distortion were available for use with the frontal view that *norma frontalis* might then receive some of the attention that has been lavished in the past upon *norma lateralis*. In the lateral film, bilaterally situated structures are superposed upon one another, and one may adopt the convention that they lie in the median sagittal plane; furthermore, the

* From the Division of Orthodontics, College of Dentistry, University of California. Presented at the International Association for Dental Research, June 21, 1947.

† Associate Professor and Chairman of the Division of Orthodontics, and Instructor in Orthodontics, respectively.

head increases little in width in postnatal growth, so that the distance from lateral film to the median sagittal plane does not increase to such an extent as does the distance from the ear-rod axis to the frontal film. Increases of this sort tend to increase object-film distance, which materially increases the degree of size distortion.

in reality a specialized drawing board and T-square, modified from the familiar prototypes to reproduce roentgen-ray paths, i.e., radii of a sphere, instead of parallel lines.

The compensator consists of two parts, a bedplate and a slider (Fig. 1). The bedplate is the equivalent of the drawing board

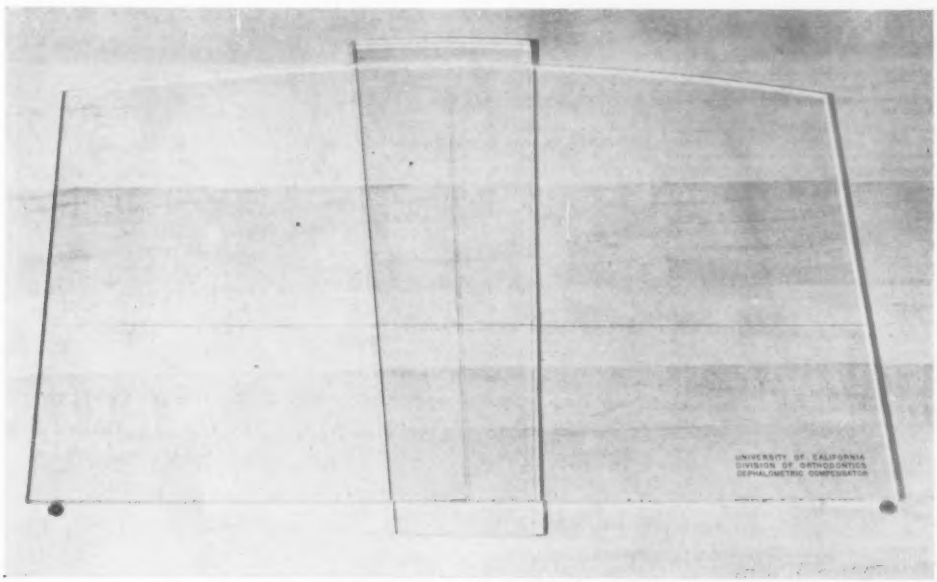

Fig. 1. The "compensator" without millimeter paper taped to the bedplate. The two engraved lines represent the axes of orientation in the Broadbent cephalometric technique; the slider traverses the curved border of the bedplate so that its edges always reproduce paths of roentgen rays.

While it is possible to make any correction desired by calculation, considerable ingenuity has been expended in efforts to provide some more convenient way of accomplishing it. The most straightforward method so far offered is that of Adams, in which he made roentgenograms of a leaded millimeter rule at progressively greater object-image distances, so that one might measure directly upon the lateral film, using a scale which was distorted to the same extent as was the image of the subject. This relies heavily upon the assumption that structures seen in *norma lateralis* are projections to the median sagittal plane, and efforts to use this method with the frontal film were less rewarding.

Our device called the "compensator" is

and is made of $\frac{1}{4}$ inch lucite. Two of the sides are parallel and at right angles to a a third side. On it are engraved two lines, one parallel to the long lower edge of the bedplate and the other parallel to the two short sides. These lines intersect at right angles in the center of the bedplate. The fourth or upper edge of the bedplate is curved and is an arc whose center is exactly 5 feet from the intersection of the engraved lines. The slider is cut to fit the curved border exactly and finished to slide smoothly along it so that it may be brought to any position on the arc. The long edges of the slider reproduce radii of the arc, regardless of the position of the slider on the arc.

In describing the use of the compensator,

we must make it clear that the films themselves are not put directly upon the bedplate for viewing; they are measured independently and the measurements themselves are taken to the compensator. Millimeter paper is taped to the bedplate so that the lines on it coincide exactly with the engraved lines. To simplify description, let us determine the true distance across the angles of the jaw. The vernier reading gives the exact distance which the film lay from the porionic axis when taken. This film plane is reproduced on the millimeter paper by a line drawn parallel to the engraved line on the compensator corresponding to the porionic axis (the longer of the two lines), and at a distance from it indicated by the vernier reading (Fig. 1). On this line the angles of the jaw are laid off as taken from the frontal film, keeping each in its proper relation to the median plane as represented by the other engraved line. The bigonial width so laid off is enlarged because of ray divergence, and must be corrected. We then bring the slider to position so that one edge lies on one point, and extend a fine line back towards the center. Since the rays which produced these images on the film traveled in straight lines as radii from the anode, the true gonial points must lie somewhere along these lines. It is a simple matter to determine precisely where they belong, using Adams' scales to measure along the Frankfort horizontal on the lateral film. To determine the true bigonial distance, measure between the two points thus established.

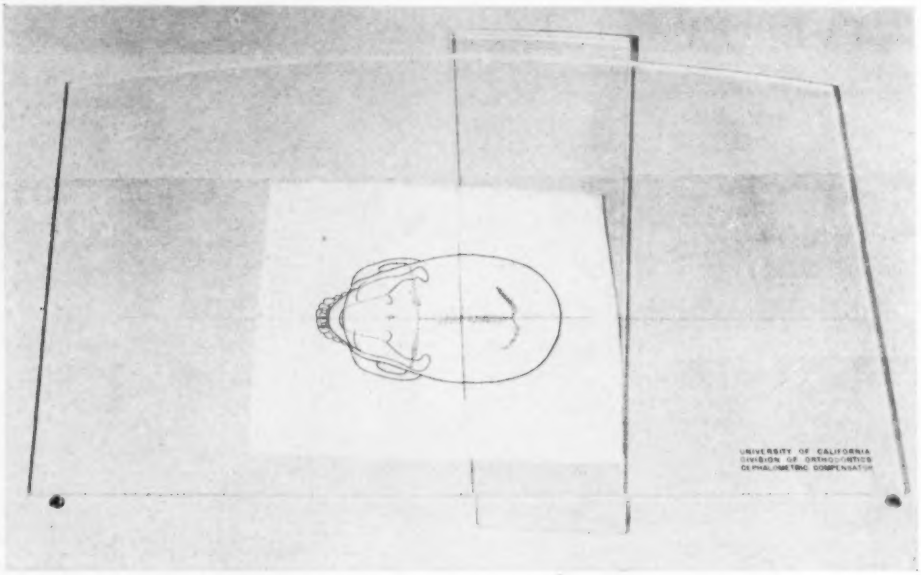

FIG. 2. Illustrating how a vertical projection of the face and cranium is created on the compensator from lateral and posteroanterior films. Unlike the images on the two films, this basal "view" is not distorted.

One will readily see that, having located these true points on the millimeter paper, we may not only measure the distance accurately between them, but we may locate a variety of other points on the paper, thus producing a third view of the skull seen at right angles to the other two, with all size distortion eliminated. This has been represented in Figure 2, but the orientation has been deliberately changed to show how the compensator may be used to correct the lateral film, so as to obtain true measurements of craniofacial depth, i.e., greatest head length, over-all jaw length, length of anterior or posterior cranial base, and so forth.

The principle described here may be put to use in techniques other than the Broadbent one to obtain quantitative values

from roentgenograms, eliminating the element of distortion introduced by the divergence of rays. This would require, of course, the construction of a compensator with an arc and slider cut to correspond with the target distance used in the particular technique. The technician chosen to do the work should be made to understand that the device is worthless unless it is made very accurately.*

SUMMARY

A simple device is described whereby one may correct for size distortion in roentgenograms, and which may be used to create a third vertical projection of the cranium when one has oriented lateral and posteroanterior roentgenograms. This vertical projection is created on millimeter paper with all distortion due to ray divergence eliminated. Incidentally, the device is a useful teaching aid in illustrating the amount of distortion inherent in a given anode-object distance when object-film distance is varied.

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* Fabrication by Plastic Productions, 809 Mission Street, San Francisco, Calif.

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Publisher: CHARLES C THOMAS, 301–327 East Lawrence Avenue, Springfield, Illinois.

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich., Office of publication, 301–327 East Lawrence Avenue, Springfield, Ill. Information of interest to all readers will be found on page vi.

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EDITORIALS

HYDROTHORAX IN CONGESTIVE HEART FAILURE

OUR clinical as well as roentgenological impressions concerning the frequency of manifestation of a certain pathological finding may be in error. For a long time there has been an impression that right hydrothorax is seen much more frequently than left hydrothorax in congestive heart failure.

McPeak and Levine[1] have recently analyzed a group of cases exhibiting congestive heart failure with hydrothorax. In order to make their analysis more significant they included only those cases suffering from clear cut cardiovascular disease with congestive heart failure. They grouped their cases under three general headings: Those exhibiting hydrothorax in congestive heart failure as shown by clinical signs and thoracentesis, and second, those exhibiting hydrothorax in congestive heart failure as shown in the roentgenological examination, and third, cases of congestive heart failure exhibiting hydrothorax at postmortem examination.

Their observations and studies led them to believe that their general impression was correct in regard to the distribution of hydrothorax in congestive heart failure and that "from whatever angle an analysis is attempted, regardless of the method of approach or the underlying cardiac condition, the combination of factors which determine the transudation of fluid into the pleural sacs exerts an influence in such a manner as predominantly to involve the right pleura. This influence, however, appears to be augmented in rheumatic heart conditions as compared to those in which failure of the left heart is more frequently encountered."

Numerous attempts have been made to explain the distribution of hydrothorax which occurs in the course of congestive heart failure, and McPeak and Levine were impressed by the fact that the subject has been approached from isolated points of view which have led to an over-emphasis of some particular factor involved, and there is a tendency toward over-simplification of the problem as a whole. They call attention to Baccelli's early work in 1867 in which he advanced the azygos theory to explain the comparative frequency of right hydrothorax, assuming that pleural fluid accumulated through disturbance in the systemic circulation and for a long time these views of Baccelli were accepted without question. However, some recent observers reporting on the more frequent occurrence of right hydrothorax explained the phenomenon by the fact that the pressure on the root of the right lung and azygos vein by an enlarged right auricle could be an explanation for a predominance of right hydrothorax, and that the site of the hydrothorax was associated with a corresponding enlargement of the right or the left side of the heart.

Other observers (Fetterhoff and Landis) presented evidence that "transudation of fluid into the pleural sacs took place from the visceral rather than the parietal layer and therefore depended upon involvement of the pulmonary instead of the systemic circulation." They were of the opinion that pressure on the right or left pulmonary veins, by a dilated right or left auricle respectively, determined the location of the pleural transudate, and since the right auricle was more easily and consequently more commonly dilated than the left, a predominance of right hydrothorax might be expected.

Other observers have presented some experimental data demonstrating a greater relative degree of pressure negativity in the

[1] McPeak, E. M., and Levine, S. A. The preponderance of right hydrothorax in congestive heart failure. *Ann. Int. Med.*, 1946, *25*, 916-927.

right pleural space, as compared to that in the left, in normal individuals, and as a result of this difference would explain the prevailing tendency toward preponderance of right hydrothorax.

Dock in 1935 presented what appeared to be convincing evidence that the anatomic and hydrostatic factors relating to the flow of blood from the pulmonary venous bed to the left ventricle strongly favored the predominance of right over left hydrothorax. He further emphasized these factors as being considerably augmented by the right lateral decubital position which cardiac patients generally prefer.

It may easily be seen that these various conjectures and observations concerning the systemic and pulmonary circulations in the pathogenesis of cardiac hydrothorax have led to much speculation and controversy. Drinker in his epoch-making contribution to pulmonary edema and inflammation stated, "It is generally acknowledged that two factors are fundamental in causing transudation in the lungs and pleural sacs. They are, first, sustained increase in pulmonary pressure, and second, anoxia—while one or the other may be dominant in a given case, they never, in my opinion, work alone. And from his studies and deductions he further stated, "It is my belief, I cannot say conviction—that simple pulmonary edema and the more serious pulmonary exudations depend more upon alterations in the permeability of lung capillaries than upon complicated pressure relations in the pulmonary circulation."

McPeak and Levine while accepting the view that the visceral pleura is the principal source of abnormal collection of fluid within the pleural sacs, and owing to their peculiar environment, their increased susceptibility to anoxia, and the inadequacy of pulmonary lymph flow under stress, that the pulmonary capillaries are particularly susceptible to the forces promoting transudation, there are yet to be considered a number of anatomical and physiological factors which may determine, modify or tend to localize such a process. These observers call attention to the fact that an explanation of the preponderance of right hydrothorax may pertain to the lungs themselves. They point out the fact that the right lung is some 10 per cent greater in volume than the left and when one considers the extra lobe of the right, the disproportion between the areas of visceral pleura on the two sides of the chest is even greater, and any factor which tends to limit respiratory excursion such as hypostasis, hepatic engorgement, cardiac enlargement, etc., tears down the natural defenses against the consequences of local increased capillary transudation.

They cite the experiments of Warren, Peterson and Drinker which showed that pulmonary lymphatic drainage takes place almost entirely through the right lymphatic duct with limited anastomosis to the thoracic duct. McPeak and Levine make the query as to what effect this might have on the lungs individually when lymphatic stasis occurs and whether the left lung receives greater benefit from the collateral drainage. They call attention to a rather important observation, namely, that it is much more difficult to form an impression as to the relative importance of the parts played by the visceral and parietal pleurae in absorption of fluid, and that little experimental work seems to have been done on which to base an opinion.

McPeak and Levine have established from an analysis of their cases that right-sided hydrothorax is much more frequent in congestive heart failure, but the causative factors which bring about this phenomenon are not readily understood. Various theories have been advanced to explain this phenomenon, none of which seem wholly adequate or satisfactory. Herein lies an opportunity for well planned research and investigation employing the roentgen ray as an adjuvant, and the recent splendid work of Macklin[2] offers a clue that will furnish a point of departure for the investigation of congestive heart failure in general and particularly the hydrothorax which so frequently accompanies it.

[2] Macklin, C. C. Terminal pulmonary venules in mammalian lungs. *Tr. Roy. Soc. Canada* (Sect. V, Biol. Sc.), 1945, *39*, 105–129. Also, Respiratory volume changes in the pulmonary blood vessels in relation to artificial relaxation therapy. *Dis. of Chest*, 1948, *14*, 534.

Srauss Peyton, Kansas City

LEWIS G. ALLEN
1891-1948

DR. LEWIS G. ALLEN, a member of the American Roentgen Ray Society since 1936 and a Past-President of the Radiological Society of North America, died in Providence Hospital, Kansas City, Kansas, on May 28, 1948.

Born in Lenexa, Kansas, in 1891, Dr. Allen was graduated from the University of Kansas School of Medicine. He served an internship at St. Joseph Hospital, Kansas City, Missouri, and at the Royal Victoria Hospital, Montreal, Canada, the latter being interrupted by his entrance into the United States Army in World

War I. Assigned to the Kansas City School of Military Roentgenology, he was with the A.E.F. as a member of Base Hospital No. 116 and Mobile Hospital No. 9.

Dr. Allen was radiologist to Bethany, Providence, and St. Margaret's Hospitals, Kansas City, Kansas, and Professor of Clinical Roentgenology at the University of Kansas School of Medicine. Dr. Allen did not limit his activities to radiology, but took a lively interest in organized medicine. He was a Fellow of the American College of Physicians, and for many years was active in the affairs of the Kansas State Medical Society. He also served as President of the Wyandotte County Medical Society, and President of the Kansas City Southwest Clinical Society. He was an honorary member of the Kansas City Academy of Medicine, and he was active in various committees and an energetic participant in local and national radiological organizations. He always demonstrated his willingness to assume responsibility and his ability to work diligently and with originality in the discharge of his duties. His was the task of formulating the plans and executing the details of the first Refresher Courses presented by the Radiological Society of North America, an undertaking which those who have had the opportunity of working with him know to have been an exacting one.

Civic affairs always claimed a great deal of Dr. Allen's time and attention. To the end he served as Chief of the Emergency Medical Service under the Civilian Defense Program for Kansas City, Kansas. He was a charter member and an active participant in the Kiwanis Club, a trustee of Group Hospital Service, Incorporated, and a member of the Board of Directors of Blue Shield.

Dr. Allen contributed numerous articles to the radiological literature and he always took an active part in the programs of medical organizations to which he belonged.

He was a sincere and loyal friend, who will be greatly missed by all his colleagues.

Ira H. Lockwood, M.D.

EDWIN LOUIS RYPINS
1903-1948

DR. EDWIN LOUIS RYPINS died on July 4, 1948, at Brokaw Hospital, Normal, Illinois. The cause of his death was skull fracture, the result of an automobile accident late Thursday afternoon, July 1. Dr. Rypins was returning from a consultation at the Veterans Facility, Dwight, Illinois, when his car was struck by a motorist who had failed to stop for an entering stop sign. He never regained consciousness.

Dr. Rypins was born in Omaha, Nebraska, on January 8, 1903, the son of Max and Natalie Rypins. He was graduated with a Bachelor of Science degree from the University of Nebraska in 1925

and from the University of Nebraska Graduate School in Medicine in 1927. His internship was served in Scranton State Hospital of Pennsylvania 1927 to 1928 and a residency in medicine was completed in Ridley Park Hospital of Pennsylvania from 1928 to 1929. Dr. Rypins engaged in general practice in Chester, Pennsylvania, 1929 to 1930. He entered the Department of Radiology for postgraduate work in radiology at Iowa State Hospital under Dr. H. Dabney Kerr in 1930 and continued his training through 1935.

In 1933 Dr. Rypins was married to Miss Martha Cannon, who survives him.

From 1936 to 1942, he engaged in the practice of radiology in Bloomington, Illinois and was appointed director of the radiological department at Brokaw Hospital, Normal, Illinois, where he served until 1942.

Dr. Rypins enlisted in the Army of the United States September 10, 1942, with the rank of Major, was promoted to the rank of Lieutenant-Colonel in January, 1945, which rank he held until the time of his discharge, October 24, 1946. His service connected activities included assignments to medical units in Louisiana and Texas from September, 1942 to March, 1943. He then served as chief of the X-ray department of the 69th General Hospital in Ledo-Assam, China, Burma and Indian Theatre and also served with the 233rd and the 9th General Hospitals on Okinawa and with the 4th and 248th General Hospitals in Manila as chief of the department. Dr. Rypins received the European Theatre Ribbon and the Asiatic-Pacific Medal with battle stars and the World War II Victory Medal and the Japan Occupation Clasp.

Following his discharge from the armed service, he returned to Bloomington and re-established his private practice and continued the directorship of the radiological department, Brokaw Hospital, Normal, Illinois and was appointed a consultant to the Veterans Facility, Dwight, Illinois.

Dr. Rypins held membership in the American Legion and the Reserve Officers Corps. He was a member of the McLean County Medical Society, the Illinois State Medical Society, where he served as Secretary of the Section on Radiology in 1948, the Illinois Radiological Society, Fellow in the American College of Radiology, American Roentgen Ray Society, Radiological Society of North America and was certified by the American Board of Radiology.

Dr. Rypins will be missed by his associates in the medical profession in Bloomington and Normal, all of whom, together with his many friends, will, with deep affection and inspiration, remember him for his judgment, his undeviating intellectual honesty, his keen wit and scientific understanding and his deep appreciation for a job well done.

E. M. Stevenson, M.D.

EDWIN S. FLARSHEIM
1894-1948

IT IS with sincere regret that we report the death on June 29, 1948, of Edwin S. Flarsheim, one of the founders of The Liebel-Flarsheim Company, Cincinnati, Ohio.

Mr. Flarsheim's death followed a long illness which had, for some years, prevented his active participation in the business which bears his name. However, his engineering genius was well known throughout the world, and his contributions to the electro-medical field will serve as a lasting tribute to his memory. To him goes the credit for the development of the great majority of roentgen-ray, electrosurgical, and electromedical equipment made by The

Liebel-Flarsheim Company for doctors, surgeons, and hospitals in all parts of the world.

Mr. Flarsheim was born in Louisville, Kentucky, on January 7, 1894. He attended Manual Training High School at Louisville, where he won high scholastic honors. Later, he graduated as top-honor engineering student from Rose Polytechnic Institute. Shortly after his graduation from Rose Polytechnic, Mr. Flarsheim joined with Mr. G. H. Liebel in 1917 to form The Liebel-Flarsheim Company. He developed the Bovie Electrosurgical Unit, L-F X-Ray Timers, L-F Potter-Bucky Diaphragms, Short-Wave Diathermy Units and many other valuable contributions to medical science.

Mr. Flarsheim's concept of human relations enabled him to develop and maintain a spirit of cooperative friendliness within the Liebel-Flarsheim organization.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Palmer House, Chicago, Ill., Sept. 14–17, 1948.

American Radium Society
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: 1949, to be announced.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Hotels Fairmont and Mark Hopkins. San Francisco, Calif., Dec. 5–10, 1948.

American College of Radiology
Secretary, Mac F. Cahal, 20 N. Wacker Drive, Chicago 6. Annual meeting: 1949, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: 1949, to be announced.

Alabama Radiological Society
Secretary, Dr. C. S. Stickley, 515 Bell Bldg., Montgomery, Ala. Next meeting time and place of Alabama State Medical Association.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Brooklyn Roentgen Ray Society
Secretary, Dr. A. H. Levy, 1354 Carroll St., Brooklyn 13, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse, N. Y. Three meetings a year January, May, November.

Central Ohio Radiological Society
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. George L. Sackett, 10515 Carnegie Ave. Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Denver Radiological Club
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida Radiological Society
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Houston X-ray Club
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. J. A. Campbell, Indiana University Hospitals, Indianapolis 7. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kansas. Meets annually with the State Medical Society.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Moris Horwitz, 441 No. Camden Drive, Beverly Hills, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Louisville Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave.,

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 323 Professional Bldg., Charlotte 2, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August. Next meeting Sept. 27, 1948.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. William Y. Burton, 242 Medical Arts Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Robert M. Lowman, Grace-New Haven Community Hospital, New Haven 11. Meets bimonthly second Thursday, at place selected by Secretary.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Edwin L. Rypins, 427 N. Main St., Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

UTAH RADIOLOGICAL CONFERENCE
Secretary, Dr. Henry H. Lerner, School of Medicine, University of Utah, Salt Lake City 1. Meets 1st and 3rd Thursdays monthly from 7:30 to 10 P.M., Salt Lake County General Hospital, September to June.

Utah State Radiological Society
Secretary, Dr. M. Lowry Allen, Judge Bldg., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. Ivan J. Miller, 49 Fourth St., San Francisco 3. Meets monthly on third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Langley Porter Clinic, University of California Hospital.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

British Empire

British Institute of Radiology Incorporated with the Roentgen Society
Medical Members' meeting held monthly on third Friday at 2:30 p.m. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 23 Welbeck St., London, W.1 England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary, Dr. E. M. Crawford, 2100 Marlowe Ave., Montreal 28, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting May 13 and 14, 1948.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad.
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 p.m.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The annual meeting of the Rocky Mountain Radiological Society, held in Salt Lake City, Utah, on August 12, 13 and 14, 1948, was a success both from its scientific and social aspects. The following were guest speakers at the meeting: Dr. L. H. Garland, Dr. John Caffey, Dr. Ross Golden, Dr. Juan A. del Regato, Dr. John D. Camp, and Dr. Wendell G. Scott.

The following officers were elected for the coming year: *President*, Dr. Howard B. Hunt, Omaha, Nebraska; *President-Elect*, Dr. K. D. A. Allen, Denver, Colorado; *First Vice-President*, Dr. M. Lowry Allen, Salt Lake City, Utah; *Second Vice-President*, Dr. Thomas B. Bond, Fort Worth, Texas; *Secretary-Treasurer*, Dr. M. D. Frazer, Lincoln, Nebraska.

SOCIEDAD DE RADIOLOGICA, CANCEROLOGIA Y FISICA MEDICA DEL URUGUAY

An announcement has recently been received from the President, Dr. Felix Leborgne, of the reorganization of the Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay. The officers of the society are: *President*, Dr. Felix Leborgne; *Vice-President*, Dr. Alfonso Frangella; *Secretary-General*, Dr. Hector Bazzano; *Secretary*, Dr. Arias Bellini; *Treasurer*, Dr. Luis Vasque Piera; *Chancellors*, Dr. Mario Cassinoni and Dr. Augustin Gorlero Armas.

THE CATLIN MARK

TO THE EDITOR:

I have recently had called to my attention an article in the quarterly review of American archaeology, *American Antiquity*, April, 1945, Volume 10, No. 4. The title of this article is "Trepanation and the Catlin Mark," and is by William H. Goldsmith.

Goldsmith would lead one to believe that the Catlin mark, as well as prehistoric trepanation, is a commonplace occurrence. However, in the literature, as far as I can find, there are only the writings of Goldsmith, and of Pepper and Pendergrass, the latter in the AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY, 1936, Volume 35, pages 1–8, and 1939, Volume 41, pages 343–346. The fact is that the Catlin mark is quite uncommon and Pepper and Pendergrass speak of it as "an erratic hereditary anomaly of ossification" and the "formation of persistent enlarged parietal foramina." With these three exceptions, this is all that I can find in the literature.

My object in writing is that a brief note appear in the AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY calling attention to the fact that it has not been recognized in the roentgenograms of the skull of over 15,000 individuals, nor has it been observed in the physical and roentgen examination of the skulls of 1,500 skeletons in the Department of Anatomy of the Washington University School of Medicine, nor was an example of it found in 200 skulls of Mound Dwellers of Missouri, Illinois, and Arkansas. Among the latter, likewise, there was no example of a trephine opening. Trephine openings have been seen in the various museums, but they are not common in any of the museums of the United States.

SHERWOOD MOORE, M.D.

AVAILABILITY OF RADIOISOTOPES WITH INCREASED ACTIVITIES

The Isotopes Division is pleased to announce that it is now possible for Oak Ridge National Laboratory to distribute irradiated units of isotopes containing larger quantities of activities, and in many cases with higher specific activity, than those listed in Radioisotopes Catalog No. 2. Previously it was necessary to limit the quantity of activity present in an irradiated unit due to available facilities for protection of personnel removing samples from the pile. Recently these facilities have improved to such an extent that this factor is no longer a limiting one.

Limitations placed on the quantity of activity which may be shipped by public carrier still must be met. In some instances, a moderate increase in total activity may be shipped satisfactorily through increasing the weight of the

shipping container. However, if abnormally large quantities of activity are requested, it generally will be necessary for the applicant to furnish a special truck or plane for transportation. The Isotopes Division will be glad to cooperate in discussing the preparation of samples with high activities and arrangements for their transportation.

Since additional time and effort is required to prepare and handle these more active samples, the allocation of these materials will be made on the basis of service irradiations, discussed on page 28 of the catalog. Therefore, samples larger than those listed for the routine units may be procured at a cost of $22 for one week irradiation, or fraction thereof, or $43 per month.

Isotopes Division Circular E-26
Oak Ridge Operations
Oak Ridge, Tennessee

ATOMIC ENERGY COMMISSION POLICY ON PRODUCTION AND DISTRIBUTION OF ISOTOPE-LABELED COMPOUNDS

Commercial firms will be encouraged to manufacture and distribute for sale tagged compounds, the radioactive materials being obtained from the Atomic Energy Commission. This is in line with the Commission's announced policy of encouraging private industry to develop the use of radioactive materials wherever industrial participation proves feasible. Certain selected compounds for which adequate commercial production does not exist, will be produced in the contractor-operated laboratories of the Commission for general distribution by the Commission. However, the Commission hopes that private firms will enter the field to such an extent that it will be able in time to withdraw from the manufacture of such compounds for general distribution.

The price to be charged for isotope-labeled compounds produced by commercial firms will be established by the firm manufacturing the material in accordance with normal industrial practices.

Inventions or discoveries made by persons using radioisotopes or using or manufacturing isotope-labeled compounds will be subject to patenting by the inventor in accordance with normal industrial practices. The Commission does not contemplate the reservation of patent rights to inventions and discoveries made by distributees who receive radioactive materials pursuant to the Commission's regular program of radioisotope distribution.

The users of radioactive isotopes or isotope-labeled compounds will be required to meet the safety and health standards that are established from time to time by the Commission. They also will be required to publish or report the significant results of investigations using radioactive materials but these reporting requirements will be applied so as not to interfere with an inventor's opportunity to obtain patent protection for his inventions and discoveries.

At present radioisotopes are sold by the Isotopes Division at a price set to cover the costs of final fabrication. This price does not cover, for example, the cost of amortizing the investment in laboratory equipment and nuclear reactors, which are used for research purposes other than radioisotope production. Consequently, the present pricing policy results in a subsidy of research in which radioisotopes are used. If and when radioisotopes are used on a large commercial scale, it may be necessary to re-examine the pricing policy.

Although the pricing formula for distributing compounds produced by the Atomic Energy Commission will attempt to include all factors directly chargeable to the production of such compounds, the resulting price may not necessarily reflect all the costs which commercial organizations must include when determining the price of their compounds.

Isotopes Division Circular E-23
Oak Ridge Operations
Oak Ridge, Tennessee

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

CANCER: DIAGNOSIS, TREATMENT, AND PROGNOSIS. By Lauren V. Ackerman, M.D., Pathologist to the Ellis Fischel State Cancer Hospital; Assistant Professor of Pathology, Washington University School of Medicine, St. Louis, and Juan A. del Regato, M.D., Radiotherapist to the Ellis Fischel State Cancer Hospital; Formerly Assistant to the Radium Institute of the University of Paris. Cloth. Price, $20.00. Pp. 1115, with 745 text illustrations and 42 color reproductions. St. Louis: C. V. Mosby Company, 1947.

Introductory chapters cover the Pathology of Cancer, Surgery of Cancer, Radiotherapy of Cancer, and a brief review of the Present Status of Cancer Research by Michael B. Shimkin of the National Cancer Institute.

The remainder of the book deals with cancer according to systems under the following headings: anatomy, incidence and etiology, pathology, clinical evolution, diagnosis, treatment and prognosis. The authors are to be commended for laying special emphasis on the clinical aspects of the various types of malignant disease and limiting the space devoted to histological pathology. All of the illustrations are of good quality, but the drawings made by Virginia Svarz Ackerman are unusually well done, particularly those which show the lymphatic drainage and paths of metastasis for each anatomical site of cancer origin. The clinical course of each type of malignant disease is described in some detail and, when possible, complicated data are placed in tables which serve to clarify the material appreciably.

To the radiation therapist, the book is disappointing. Although one of the authors is an authority on this type of therapy, no detailed techniques are set down and, for the most part, the subject is covered in a very general manner. It is also to be regretted that the authors express a prejudice against radium therapy apparently based on a lack of experience with this method. The following quotations will find little favor with competent radium therapists: "An accurate dosimetry is not possible with the use of radium," "Interstitial curietherapy is an expeditious method of treatment which is only justified in small lesions," "Interstitial application of radium element needles or radon seeds has been almost universally abandoned as a method of treatment of primary carcinomas of the lower lip," "Carcinoma of the tongue is one of the few remaining, if not the last, lesion for which this form of treatment is indicated." Having shown such a lack of confidence in the efficiency of radium, the authors express a surprising faith in roentgen therapy as evidenced by the following statement: "External roentgentherapy is capable of sterilizing metastatic carcinoma [in lymph nodes] from a primary lesion of the lower lip."

In spite of these defects, the general description of the appearance and behavior of the various types of cancer are so well done that every radiologist interested in therapy will find this book a very useful storehouse of information made readily available in a single volume of moderate size.

CHARLES L. MARTIN, M.D.

HODGKIN'S DISEASE AND ALLIED DISORDERS. By Henry Jackson, Jr., A.B., M.D., Assistant Professor of Medicine, Harvard Medical School; Associate Physician, Thorndike Memorial Laboratory, Boston City Hospital, and Frederic Parker, Jr., A.B., M.D., Associate Professor of Pathology, Harvard Medical School; Pathologist-in-Chief, Boston City Hospital. Cloth. Price, $6.50. Pp. 177, with 15 plates. New York: Oxford University Press, 1947.

In seven chapters, this important contribution to the subject of lymphoblastoma and lymphomatoid conditions deals at some length with Hodgkin's disease, reticulum cell sarcoma, lymphocytoma and lymphoblastoma, lymphosarcoma, giant follicle lymphoma, plasmocytoma, and endothelioma. The book is well printed and well bound in dark red buckram, and the quality of most of the illustrations is excellent.

Essentially this book, which does not deal exhaustively with the subject as far as a review and analysis of earlier writings are concerned, is an attempt of the authors to set forth their

personal views in relation to the clinical and pathologic phases of the problem. Perhaps the main feature of this work, and one which will attract most attention, is a new classification according to which Jackson and Parker claim to recognize three distinct forms of Hodgkin's disease: paragranuloma, Hodgkin's granuloma, and Hodgkin's sarcoma. This distinction, of course, is based purely on pathologic grounds (microscopic observations) and, for this reason, it probably must be attributed or credited to Parker. Without any doubt, this will stir up quite a controversy, because a great many pathologists will be unable to accept Parker's views in this respect. But sometimes controversy is valuable because it tends to stir sluggish minds to greater activity and to closer observation; and this might well result in the accumulation of greater knowledge.

Readers who have had substantial experience with this group of diseases will immediately question whether Jackson and Parker's "paragranuloma" deserves to be regarded as an independent entity. In relation to the symptoms and course of Hodgkin's disease, these readers will say, quite justly, that the reason for the absence of any symptoms in the condition which Jackson and Parker call "paragranuloma" is that the affected lymph nodes have not yet enlarged sufficiently to cause symptoms; in other words, that the morbid process is in an early stage when it would not be likely to produce symptoms. Against this, some would advance the objection that the long duration of paragranuloma in the small number of cases cited as examples would be against these being cases of true Hodgkin's disease. This, of course, is a misconception based on earlier writings which, in turn, were based on cases in which the malignant lymphoid process had reached an advanced stage. Those who have seen a large number of authentic cases know full well that, in a certain percentage, the patients can survive many years.

The statistics given by Jackson and Parker have not as much value as they might have, and this is also true of most of the statistics which have been published until now. Pathologists and many other physicians have a tendency to believe that necropsy findings must necessarily be accurate; but conditions which are found after death, while they are accurate as far as they go, may not represent a state of the lymphatic system and of other organs which may have been present some time before and which, during the terminal period of the patient's life, may have diminished or disappeared. As far as the lymphatic system is concerned, this is much more common and more important than is generally realized.

Another flaw—if flaw it can be called—relates to the case histories cited as examples of one phase or another. Jackson and Parker appear to have accepted at face value the histories which had been written by the attending physicians. But on reading these, anyone who has had an extensive experience of cases of this kind would know that, in all probablity, many of the patients had had, for many months or many years, other symptoms which had been disregarded or the cause of which had not been recognized.

The authors also seem to have accepted without question the statements of patients that enlarged lymph nodes in the neck had been the first manifestation of the disease, and from this they have assumed that Hodgkin's disease nearly always begins in the cervical nodes. This is an ingenuous and uncritical attitude which is all too common, but it does not happen to be true. Because the neck is such a prominent and accessible part of the body, because while shaving men have an exceptional opportunity to see the neck, and because women are greatly concerned with the appearance of their necks, it is only natural that any blemish or lump in this region should attract attention. But when some of the cervical nodes become abnormally large, a critical analysis of the circumstances will show that the cervical nodes are affected secondarily as often as they are affected primarily.

Compared with the other chapters, the chapter dealing with lymphosarcoma is quite brief. Apparently Jackson and Parker restrict the diagnosis of lymphosarcoma much more than do the majority of pathologists. How these will react to this exclusive attitude remains to be seen. Unless all signs fail, coming meetings of pathologists should be interesting.

Nevertheless, this book is a valuable contribution and deserves a careful study.

A. U. Desjardins, M.D.

Practical X-Ray Treatment. By Arthur W. Erskine, M.D. Third edition, revised and enlarged. Fabrikoid. Price, $4.50. Pp. 155, with 22 illustrations. Saint Paul and Minneapolis: Bruce Publishing Company, 1947.

This is a small volume closely packed with well chosen information and, as the author

states, it is not intended as a textbook for those well informed in this field. The fundamentals of equipment are well brought out, an excellent description is given of scattered radiation, and sufficient clinical information is included to give the novice a good idea of the problems involved.

The chapter entitled "The Cancer Problem and the Radiologist," could profitably be read not only by every radiologist, but by every practicing physician.

If there is any criticism directed against this book, it is simply that the author has made the subject seem so easy that those who are not qualified to do roentgen therapy may receive from it a false sense of security.

This should be a highly satisfactory compend for undergraduate medical students who wish to purchase a book on each subject while they are still in college, with the idea of building up a library for future study.

Robert B. Taft, M.D.

BOOKS RECEIVED

Hodgkin's Disease and Allied Disorders. By Henry Jackson, Jr., A.B., M.D., Assistant Professor of Medicine, Harvard Medical School; Associate Physician, Thorndike Memorial Laboratory, Boston City Hospital, and Frederic Parker, Jr., A.B., M.D., Associate Professor of Pathology, Harvard Medical School; Pathologist-in-Chief, Boston City Hospital. Cloth. Price, $6.50. Pp. 177, with 15 plates. New York: Oxford University Press, 1947.

X-Rays and Radium in the Treatment of Diseases of the Skin. By George M. MacKee, M.D., Professor of Clinical Dermatology and Director of Department of Dermatology (Skin and Cancer Unit), New York Post-Graduate Medical School and Hospital, Columbia University, and Anthony C. Cipollaro, M.D., Assistant Professor of Dermatology and Assistant Director of Department of Dermatology (Skin and Cancer Unit), New York Post-Graduate Medical School and Hospital, Columbia University. Contributor: Hamilton Montgomery, M.D., Associate Professor of Dermatology, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minn. Fourth edition, thoroughly revised. Cloth. Price, $10.00. Pp. 668, with 321 engravings and 4 colored plates. Philadelphia: Lea & Febiger, 1946.

Radium Dosage: The Manchester System. Edited by W. J. Meredith, M.Sc., F. Inst. P., Christie Hospital and Holt Radium Institute, Manchester. Cloth. Price, $4.50. Pp. 124, with 38 figures and 4 plates, and numerous tables. Baltimore: Williams and Wilkins Company, 1947.

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Vol. IV. 1943–1944. Cardboard. Price, 16s. Pp. 379, with numerous illustrations. London: Royal Cancer Hospital (Free), 1947.

Textbook of Endocrinology. By Hans Selye, M.D., Ph.D. (Prague), D.Sc. (McGill), F.R.S. (Canada), Professor and Director of the Institut de Médecine et de Chirurgie expérimentales, Université de Montréal. With a Preface by Professor Bernardo A. Houssay, Prix Nobel, 1947, Buenos Aires, Argentina. Cloth. Price, $10.24. Pp. 914, with numerous illustrations. Montreal, Canada: Acta endocrinologia, Université de Montréal, 1947.

Endogeneous Endocrinotherapy Including the Causal Cure of Cancer. Compendium by Dr. Jules Samuels. Specialist for endogeneous endocrinotherapy, Amsterdam. Cloth. Pp. 539, with 30 illustrations. Amsterdam, Netherlands: Holdert & Co., 1947.

Concise Anatomy. By Linden F. Edwards, Ph.D., Professor of Anatomy, The Ohio State University, Columbus, Ohio. Cloth. Price, $5.50. Pp. 548, with 324 illustrations. Philadelphia: The Blakiston Company, 1947.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Simmons, D. R., and Peyton, W. T. Premature closure of the cranial sutures. *J. Pediat.* Nov., 1947, *31*, 528–547.

Craniostenosis is a relatively rare anomaly characterized by premature closure of the cranial sutures. There are many variations dependent on which sutures show early closure. Surgical intervention in the condition has been frequently tried but would be more successful if indications were more carefully considered and suitable operations employed. It is important that bony regeneration across operative defects be prevented.

Virchow first described craniostenosis in 1851. Von Graefe, in 1866, was the first to recognize the importance of craniostenosis in visual impairment. Lannelongue, in 1890, was the first to attempt operative correction of craniostenosis by removing strips of bone along the prematurely fused sutures. Jacobi emphasized that the operation should not be employed in true microcephaly.

Normally a slight separation of the cranial sutures is present at birth but by the end of the sixth month firm fibrous union is present. The posterior fontanelle should be closed by the sixth week and the anterior fontanelle by the sixteenth month. The growth of the skull and the obliteration of the cranial sutures depends on brain growth. In microcephaly premature fusion of all the sutures and the fontanelles occurs; in hydrocephalus both are delayed.

If unilateral brain atrophy is present in infancy the same side of the skull will be smaller. After the age of three only slight increase in the intracranial capacity occurs and any increase in size of the skull must be due to increased thickness and growth of the sinuses and facial bones. It has been demonstrated experimentally that cranial bones grow in a lateral direction from the suture lines which explains why, following premature synostosis of a cranial suture, growth ceases perpendicular to that suture.

Much confusion in terminology exists in classification of premature closure of the intracranial sutures. The authors suggest the following simplified classification:

A. Complete, early, premature synostosis of the cranial sutures (oxycephaly, turricephaly, türmschädel).
   1. Oxycephaly without facial deformity.
   2. Craniofacial dysostosis of Crouzon.
   3. Acrocephalosyndactylism.
   4. Delayed oxycephaly (onset after birth).

B. Incomplete early synostosis of the cranial sutures.
   1. Scaphocephaly: premature closure of the sagittal suture.
   2. Brachycephaly: premature closure of the coronal suture, or of the coronal and lambdoidal sutures.
   3. Plagiocephaly: premature asymmetrical closure of the sutures.
   4. Mixture.

C. Late premature synostosis of the cranial sutures after the skull has reached or nearly reached adult size.

Various causes for craniostenosis have been proposed such as meningeal inflammation, heredity, rickets, lues, glandular disturbance, and birth trauma. However, the true cause remains unknown. Craniostenosis occurs five times as often in males as in females. If the suture occurs after the age of three no symptoms should result. The resultant shape of the head depends upon the sutures involved. Early closure of the sagittal suture results in dolicocephaly; premature closure of the coronal suture results in brachycephaly. Closure of all sutures results in turricephaly from upward expansion against the patent anterior fontanelle.

Early recognition is important if surgical correction is to be effective. Common associated findings include exophthalmos from shallow orbits, divergent strabismus, saddle-shaped nose, prognathism, high arched palate and dental defects as seen in Crouzon's type of dysostosis. Other associated deformities may include hypertelorism, syndactylism, optic atrophy, convulsive seizures and various degrees of mental deficiency.

Roentgenograms will demonstrate the obliterated sutures with increased density and

thickness of the adjacent bone. The abnormal shape of the skull is more apparent by roentgen examination than on physical examination, particularly in older children. Shallow orbits, steep orbital roofs, a deep middle fossa, a short narrow orbital fissure and small frontal sinuses are all usually present. The basilar angle is decreased in oxycephaly and increased in scaphocephaly.

The authors discuss in some detail the means of operative correction.

The prognosis for life is dependent on the severity of the disease. Most patients will exhibit some mental deficiency. Optic atrophy and blindness are common dangers.—*Rolfe M. Harvey, M.D.*

Watson, Charles W., Murphey, Francis, and Little, Samuel C. Schistosomiasis of the brain due to Schistosoma japonicum. *Arch. Neurol. & Psychiat.*, Feb., 1947, *57*, 199–210.

The deposition of ova in the central nervous system is a rare complication of the infection in man. The authors review the literature obtaining to this condition and report in detail their findings in a patient in whom ova of *Schistosoma japonicum* were found in the brain.

The date of the patient's exposure to infected water was definitely known. About ten days later, he developed the typical signs and symptoms of infestation by *Schistosoma japonicum*.

The first cerebral seizure developed approximately 156 days following the original exposure to the parasite. Headache, loss of consciousness, confusion, aphagia and jacksonian attacks characterized the cerebral seizures. A space-taking lesion was localized in the left parieto-temporal region. At operation, a tumor mass was found which was thought to be a glioma. As the lesion was extensive, a biopsy was removed and a subtemporal decompression performed.

Histopathologically, the mass proved to be due to a granuloma which contained the *Schistosoma japonicum*. Because of this, active specific chemotherapy was begun.

The seizures continued in spite of large amounts of fuadin. The patient was therefore operated upon a second time four months later when it was noted that the lesion had disappeared, leaving behind a large area of scar tissue. Whereas at the first operation, marked compression of the lateral ventricle due to the granuloma was noted, at the second operation, it was obvious that the formerly compressed lateral ventricle had become greatly dilated.

The patient's general condition improved following the second operation and the seizures were becoming less frequent and less severe when the patient was last seen.

Excellent photomicrographs of the patient's cerebral lesion and a reproduction of the ventriculogram enhance the value of this important contribution.—*Philip J. Hodes, M.D.*

Hodgson, H. K. Graham. Cholesteatomata of the temporal bone. *Brit. J. Radiol.*, May, 1947, *20*, 202–204.

The development of a cholesteatoma requires a low grade chronic infection in a diploetic or poorly pneumatized mastoid. When the infection is virulent it either spreads through the antrum to the mastoid cells in a cellular mastoid, or in an acellular mastoid it infiltrates the bone producing a diffuse bone infection. On the other hand, in the case of a less virulent infection the progress is much slower. The normal mucosa of the tympanum is destroyed and replaced by epidermal cells. By a continuous process of desquamation and replacement the mass of debris enlarges. Bone is destroyed not by inflammation but by pressure erosion. The smallest part of the space in which this mass is enlarging is the aditus ad antrum, and therefore bony changes are frequently seen here first. With further enlargement the mass may erode through its containing wall. Perforations through the tegmen enter the middle fossa; in other directions the fistulae develop between the labyrinth of the external auditory canal.

In the roentgenogram cholesteatomas appear as areas of rarefaction in usually dense bone, which are less transparent than air cells of corresponding size would be. Usually these are in the region of the antrum and the margins are usually smooth, but in the presence of a few scattered cells the outline may be quite irregular. In the posteroanterior oblique views the destruction should be sought near the apex of the external canal. In oblique lateral views it is seen in the area between the tegmen tympani and the upper part of the posterior wall of the external auditory canal.

Mastoid abscesses are also areas of destruction but are usually found in the peripheral zone of the mastoid, and they are more common in a cellular mastoid. Cholesteatoma oc-

curs almost invariably in an acellular or poorly pneumatized mastoid.—*E. F. Lang, M.D.*

WELIN, SÖLVE. The x-ray diagnosis of cholesteatoma in the temporal bone. *Brit. J. Radiol.*, May, 1947, *20*, 192–201.

A cholesteatoma is transparent to roentgen rays and can be demonstrated only when it has produced bone changes. Minor bone changes can be appreciated only by examination of standard, accurately made views of the mastoid with a detailed knowledge of the normal structure of the temporal bone. Both mastoids should be examined, and the films should include the following projections or modifications: fronto-occipital (Towne) projection, oblique lateral (Law) projection, submentovertical projection, and a projection with the long axis of the petrous pyramid parallel to the film (as the Stenvers).

Although cholesteatomas are sometimes easily demonstrated in sclerotic or even diploic mastoids, the presence of considerable pneumatization complicates the picture. In these cases it is important to remember that a negative examination does not exclude the possibility of the existence of a cholesteatoma.

When the mass of epithelial cells develops in the external canal the otologist usually refers the patient for roentgen examination only if there is a question as to the extent of the lesion. In this situation the tumor might erode the posterior wall or floor of the external canal and be visible in a Law projection and in a submentovertical view.

A cholesteatoma in the attic may produce one of three types of destruction, depending on its position. On the lateral wall it produces characteristic spike-like or rounded defects in the lower margin of the attic. In the roof it produces destruction upward toward the middle fossa. In submentovertical projections this destruction is shown and frequently remnants of the ossicles may be seen. A large percentage of cholesteatomas erode posteriorly, enlarging the aditus ad antrum. In almost half of all cases of cholesteatoma this enlargement of the aditus can be demonstrated. It must be remembered that these changes show only the presence of the lesion, and not its extent, as it may go on into the antrum or forward into the tympanum without producing further destruction.

In involvement of the antrum, the cholesteatoma usually must become quite large to produce destruction. This type (if not shown by concomitant enlargement of the aditus) is demonstrated most easily in films in the Towne projection. If the antral cholesteatoma is situated in a well pneumatized mastoid it may not be demonstrable.

Small cholesteatomas may produce no changes, or at best, minimal changes in the aditus. Large ones may be confused at times with mastoid abscesses, although clinical differentiation is not so difficult.—*E. F. Lang, M.D.*

NECK AND CHEST

MASSOPUST, LEO C. Infrared photographic study of the superficial veins of the thorax in relation to breast tumors. *Surg., Gynec. & Obst.*, Jan., 1948, *86*, 54–58.

In this preliminary report on the use of infrared photography in the diagnosis of breast tumors a simple technique using a Wratten No. 87 filter, infrared film and flat incandescent illumination is briefly described.

Tumors alter the pattern of the superficial veins of the breast and in an encouraging number of cases the pathologic diagnosis confirms the photographic findings. In several malignant cases the photographs revealed unilateral wrinkling below the nipple and other slight distortions which were difficult or impossible to see with the naked eye.

Study of more cases by the method is indicated to evaluate its usefulness as an adjunct in the detection and classification of breast tumors.—*J. L. Boyer, M.D.*

ABRAMSON, W., and WARSHAWSKY H. Cancer of the breast in the male, secondary to estrogenic administration; report of a case, *J. Urol.*, Jan., 1948, *59*, 76–82.

Estrogenic therapy for prostatic carcinoma is an accepted procedure. The effect is apparently due to inhibition of the trophic functions of the anterior pituitary which causes decreased stimulation of adrenogenic glands. Cancer of the breast has been produced experimentally in male mice by estrogenic injections. Patients receiving estrogenic therapy frequently develop painful swollen breasts. Previous reports of the development of breast cancer in females receiving estrogenic therapy have been made but no previous reports in males.

The dosage of stilbestrol used in this type of therapy is discussed and the authors then report the case of a fifty-one year old colored male

who was admitted to the hospital for a painful back. Roentgen studies showed multiple metastatic lesions of the spine and femurs and pelvis from prostatic carcinoma.

The patient was given 1 mg. of stilbestrol daily for approximately eighteen months following refusal of orchidectomy. At the end of this period both breasts showed definite hypertrophy but no axillary adenopathy was noted. At this time a bilateral orchidectomy was performed. Following operation the patient was discharged with the advice to continue his stilbestrol therapy. Approximately six months later several hard nodules were palpated in both breasts. Death occurred three months later at which time an autopsy revealed bilateral extensive carcinoma of the breast with axillary metastases.

The authors do not advise discontinuance of estrogenic therapy in prostatic cancer but do recommend careful frequent examination of the breasts in cases undergoing such therapy and discontinuance of the therapy if nodules develop in the breasts.—*Rolfe M. Harvey, M.D.*

Sweet, R. H., Findlay, C. W., and Reyersbach, G. C. The diagnosis and treatment of tracheal and esophageal obstruction due to congenital vascular ring. *J. Pediat.*, Jan., 1947, *30*, 1–17.

Double aortic arch was considered a pathological curiosity prior to 1925. Medical treatment is not satisfactory. Patients die of suffocation or repeated pulmonary infarcts or are forced to live on soft or liquid diets. Surgical intervention was suggested by Sprague in 1933. The author discusses in detail 2 illustrative cases.

The first case was that of a $3\frac{1}{2}$ month old male infant who was admitted for a paroxysmal cough and wheezy breathing which had been present since ten days after birth. Recurrent attacks of cyanosis had also been noted. A chest roentgenogram showed increased hilar density and a diagnosis of virus pneumonia was made. The patient became cyanotic during a feeding spell and was transferred to the Massachusetts General Hospital.

Roentgenograms showed a posterior indentation of the barium-filled esophagus at the level of the aortic arch and an indentation of the right lateral border of the esophagus at a slightly more distal level. The impression was right-sided aortic arch and a vascular ring about the esophagus and trachea. At operation a double aortic arch was found and an anomalous left innominate artery which arose from the left aortic arch. A patent ductus arteriosus was also present connecting the left aortic arch to the pulmonary artery. The patent ductus and the left aortic arch were ligated and divided. This resulted in freeing the esophagus and trachea from their previous constriction.

Following operation dysphagia was no longer noted and breathing was normal except for slight cyanosis with crying spells. Postoperatively a bronchogram showed slight indentation of the right side of the trachea by the right aortic arch and sharp deviation of the trachea to the right just distal to this. The left main bronchus emerged from the trachea at an acute angle and was constricted in its midportion. The authors discuss the embryology of the great vessels of the heart showing why reported anomalies occur.

Case II was that of a nine month old male who had had a persistent loose cough since discharge from the maternity hospital. The cough gradually became worse and the patient began to vomit feedings. A roentgenogram of the chest showed a prominence of the upper mediastinal shadow on the right. A barium swallow at the age of two showed displacement of the superior mediastinum to the right and narrowing of the trachea, posteriorly, at the level of the aortic arch and on the right. A vascular ring encircling the trachea and esophagus was considered the probable diagnosis. At the age of four this diagnosis was confirmed by demonstration of anterior and posterior compression of the esophagus and anterior displacement of the trachea. At operation a double aortic arch was found and the right aortic arch was ligated and severed. This case was apparently a mirror image of the first and the embryological development is fully discussed and illustrated.

The differential diagnosis of respiratory stridor in infants is then discussed. Emphasis is placed on the diagnosis of double aortic arch as a possible cause, especially when aggravated by swallowing. A summary of the pertinent roentgen findings in double aortic arch includes the following: widening of the superior mediastinal shadow to the right on the posteroanterior film of the chest, absence of the aortic knob on the left, lateral indentation of the barium-filled esophagus, posterior indentation

of the esophagus, forward and lateral displacement of the trachea and esophagus, and narrowing of the trachea as demonstrated by bronchography.

The surgical approach is also discussed. Early operation is advisable once the diagnosis is established, although it is possible that symptoms may never develop.—*Rolfe M. Harvey, M.D.*

ROENTGEN AND RADIUM THERAPY

PFAHLER, GEORGE E., and KEEFER, G. P. Roentgen therapy in chronic mastitis. *Pennsylvania Med. J.*, Sept., 1947, *50*, 1347–1356.

Chronic mastitis has also been described as mazoplasia, chronic cystic mastitis, fibrocystic mastitis, adenofibrosis, and Schimmelbusch's disease. It is characterized by pain and tenderness, usually preceding the menstrual period, and by diffuse or localized nodularity of the breasts. Ewing believed that the disease begins as an inflammation or functional hypertrophy and often ends as a neoplasm. On the basis of a chronic inflammatory productive process, roentgen therapy is useful as such inflammatory processes in general have been found to yield to irradiation.

We nearly always find a nodular or local increased density over the painful area, and most often it involves the upper outer quadrant. Sometimes a localized nodule or more prominent irregular mass is found which suggests carcinoma. If there are associated smaller areas of induration, and if the opposite breast is involved, even to a much less extent, and if the symptoms are definitely associated with or precede the menstrual period, one is justified in treating it as a chronic mastitis, but probably not for more than a month or two unless there is some definite improvement. A discharge from the nipple is at times associated with chronic productive mastitis and may be the only symptom. If this is serous in character, it is not likely to indicate cancer. This discharge commonly is arrested by irradiation, but if it is bloody, one must be cautious as it may signify cancer.

The authors realize that clinical judgment or clinical diagnosis without biopsy or mastectomy cannot be absolutely reliable. Neither can a small amount of tissue removed in these cases for microscopic study or puncture biopsy be reliable, for it has been shown that carcinoma is more apt to be found in the small nonpalpable cysts than in the larger ones, also that removal of a large cyst for diagnosis may leave the small carcinomatous cyst in the breast. Where possible, cases should be seen jointly by radiologist and surgeon.

Of the 151 cases treated by one of the authors 30 had local excisions of the tumor tissue, and in these 30 cases which were considered doubtful only one showed cancer. Of these 151 cases, 111 showed complete recovery and an additional 35 cases have shown very marked improvement or practically recovery, leaving only 2.6 per cent of failures. From the fact that only one out of 151 patients with diseased breasts developed cancer of the breast, the authors conclude that the clinical diagnoses were extraordinarily accurate or the treatment prevented the development of carcinoma in some of the cases.

The treatment of this condition differs markedly from that for cancer in which case the technique is identical with that given for preoperative treatment. In chronic mastitis the authors aim to give as little treatment as is possible for satisfactory results. Therefore, they confine the treatment to the palpable disease or to the painful tender areas. They usually only need to give from four to six treatments. Usually the treatment is given through a 6 by 8 cm. field, and because the upper outer quadrant is most often involved, they begin in that area. The second treatment is given a week later from the opposite side of the breast. The third treatment is given two weeks later, and then four weeks apart for the fifth and sixth treatments. Each treatment represents a 50 per cent erythema dose, using high voltage rays.—*K. K. Latteier, M.D.*

BACLESSE F. Radiothérapie des cancers du larynx (endolarynx); résultats éloignés obtenus dans 341 cas irradiés à la Fondation Curie. (Radiation therapy of cancer of the larynx (endolarynx); end results obtained in 341 cases irradiated at the Curie Foundation.) *J. de radiol. et d'électrol.*, 1946, *27*, 63–64.

This statistical study, one of the most interesting published up to the present day, consists of 341 cases of cancer of the "endolarynx." This term is used to mean cancers of the larynx *excluding* those of the hypopharynx, the aryepiglottic fold, and those of subhyoid involvement of the epiglottis. All reported were treated

between 1919 and 1940 and have a minimum follow-up period of five years. A large number of these cases were treated by Dr. Coutard (or under his direction) up to 1937. Histopathologically, the lesions were epitheliomas. Two sarcomas were excluded from this series. Among these 341 cancers were 16 females of which 6 remained cured. The total of complete cures for all cases irradiated during the twenty-one years was 17 per cent (59 cures in 341 cases). This figure includes all the cases treated by roentgen rays and radium and includes those receiving postoperative irradiation following hemilaryngectomy or complete laryngectomy. Two hundred ninety-nine cases treated by roentgen ray gave 58 cures. Forty-two cases treated by radium gave a single cure (one woman).

From the standpoint of extent of lesion and adenopathy the following number of cures was obtained:

Cancer without adenopathy and confined locally to the vestibule, vocal cords, or subglottic area: 40 per cent cure (20 cures in 51 cases). Extensive lesions without adenopathy: 18 per cent (35 cures in 189 cases). Extensive lesions with adenopathy: 4 per cent (2 cures in 49 cases). Lesion in subglottic region: (1 cure in 14 cases).

These statistics are established in a rigid manner since they include *all* cases treated and patients apparently cured, but dead of an intercurrent disease before five years, are counted as a failure.

The results obtained in the course of the last year of this study (1940) can better measure the progress realized than can the study of the entire series which is necessarily affected by technical and clinical errors in the earlier years. In 1940, in 33 treated laryngeal cancers 13, or 39 per cent, remain cured after five years. Cancers of the vestibule, all of which had rather extensive involvement, gave 14 per cent cure (2 cures in 14 cases). Cancers limited to the vocal cord were all cured: 100 per cent (5 cures in 5 cases). No cancer in the subglottic region was irradiated in 1940, this variety being reserved for surgery exclusively.

The author believes that the progress obtained in the results of radiation treatment of laryngeal cancer over the years 1919–1940 in his institution is due to: (1) utilization of small fields which are progressively reduced in size toward the end of the series of treatments, and (2) the increase in total duration of treatment. This fractionation (6–8–10–12 weeks) has been used regularly during the past six years.—*William M. Loehr, M.D.*

MISCELLANEOUS

Lamarque, P. Une visite aux laboratoires américans de radiologie à la fin de la guerre. (A visit to American laboratories of radiology at the close of the war.) *J. de radiol. et d'électrol.*, 1946, *27*, 40–46.

The author reports on a four months' visit to the United States and Canada between June and October, 1945. To the American radiologist, so accustomed to steady, uninterrupted, and unexcelled technological advancement, this article by Dr. Lamarque underlines the recent outstanding American achievements immediately apparent to a European visitor. It is good to see an appraisal of our advantages and our work through the eyes of a foreign colleague.

His comments cover: (1) Roentgenologic apparatus—our excellent rotating-anode tubes, control panels mounted on the wall (in contrast to cumbersome control stands taking up floor space in European departments), our more widespread use of stereoscopic films, the use of the phototimer and photofluorography, the better quality of film emulsions in U. S. films than in European films even before the war, the work and apparatus making cardioangiography possible, the supervoltage roentgen therapy equipment at Memorial Hospital (1,000–2,000 kv., peak), the van de Graaff type at Boston, the Kerst betatron and the great numbers of cyclotrons throughout the United States. The author says, "At the present time there is a cyclotron almost everywhere." (2) Radium therapy—radium therapy here differs little from that in France, the most striking items here being the radon gold seeds, the ingenious device of Failla's for preparing the gold seeds, and, of course, the very convenient dosage tables of Failla, Quimby and Marinelli. (3) Dosimeters—the general availability of Victoreen r-meters in nearly all departments and offices and the great number of full-time physicists attached to hospital departments as well as large numbers of radiation physicists available for calibrating roentgen therapy apparatus throughout this country. (4) Radiotherapy techniques—as everywhere throughout the world, techniques of radiation treatment vary from place to place and from school to school. The author felt that in the United

States there is, in general, less preoperative and postoperative irradiation for cancer of the breast than in his own country. He was also struck by the great variations in treatment techniques for cancer of the larynx, as to when surgery was resorted to, the variations in extent of surgical attack and lymph-node dissection. Details of three different major methods of irradiating cancer of the larynx in three large radiation centers in the United States are given, namely, those of Dr. Martin at Memorial Hospital, Dr. Lenz at Columbia Medical Center, and Dr. Cutler at Tumor Institute, Chicago. (5) Therapy of cancer of the uterine cervix—in the United States this type of cancer seemed to the author to be treated according to two general methods based upon two influences, the school of thought championed by the Radiumhemmet of Stockholm, and that of the Institute of Radium at Paris, the one using a massive dose of radium for a short time and the other a less massive dose over a more prolonged period. The author felt that in our country more therapists followed the Stockholm school. (6) Laboratories of pure research—the work of Marinelli at Memorial Hospital on radioactive iodine and of Quimby at Presbyterian Hospital with radioactive sodium in studying patients with vascular lesions by tracer technique is well summarized. The list ends with an emphasis on the importance of the work of Quimby. Failla, Marinelli and White on the establishment of the gamma-roentgen as a means of more correctly expressing the dose absorbed by the tissues. Much of the research being carried on at the Radiation Laboratory at Berkeley, California, was not accessible to the author as the Unted States was still practically at war (July to October, 1945).

Dr. Lamarque visited radiological departments in Philadelphia, New York City, Boston, Rochester (N. Y.), Cleveland, Detroit, Chicago, Minneapolis, The Mayo Clinic, San Francisco and Los Angeles and in each place found a cordial reception and felt that American physicians have an affection for his country which his countrymen should not underestimate.

Dr. Lamarque is the abstractor of the American radiological literature for the *J. de radiol. et d'électrol.*—*William M. Loehr, M.D.*

REIDY, JOHN A., LINGLEY, JAMES R., GALL, EDWARD A., and BARR, JOSEPH S. The effect of irradiation on epiphyseal growth. II. Experimental studies upon the dog. *J. Bone & Joint Surg.*, October, 1947, *29*, 853–873.

Studies previously completed on the young rat by the authors showed that it was possible to impede growth in the long bones by exposing the epiphyseal cartilages to roentgen irradiation. These investigations demonstrated clearly that, with dosages of between 665 r and 1,165 r the epiphyseal cartilage was affected profoundly. The adjacent tissues—such as synovial membrane, articular cartilage, cortical bone, bone marrow and skin—evinced morphological changes of minor import.

To verify the results of the rat experiments and to expand the scope of the animal investigations, it seemed advisable to do a similar study on dogs. These experiments were undertaken because of their possible therapeutic application to man.

Roentgen dosages of from 800 to 1,200 r were directed over selected joints of six-week-old dogs. The treated area included the joint, epiphysis and adjacent metaphysis. The epiphyseal cartilage was profoundly affected, and retardation of growth occurred. The articular cartilage of the treated joints showed frank microscopic evidence of degenerative changes, and was not as thick as in the controls. These changes were not sufficient to interfere with joint function during the period of the experiment, and were not apparent on gross examination. There was no evidence of significant abnormality in the adjacent cortical or cancellous bones, synovial membrane, joint capsule, skin or periarticular soft tissues. In 8 of 12 animals, mild bowing of the treated forelimb occurred. No such deformity occurred in the hind limbs. Although shortening of the treated bone occurred in each instance, there was stimulation of growth at the untreated epiphysis of the treated long bone. The cause of this stimulating effect was not apparent.

The authors conclude that the clinical use of roentgen irradiation of growing epiphyses to control longitudinal growth inequalities in children must be considered as experimental, and fraught with some potential dangers. Whether the danger is greater than is incurred in surgical procedures such as lengthening or shortening of the lower extremity and epiphyseodesis, must await further investigation.—*R. S. Bromer, M.D.*